Open NSH-BMT Protocols: For questions regarding eligibility, please call Stacy Brown, Clinical Research & Data Supervisor, (404) 851-8238 or stacey.brown@northside.com

	NSH IRB-BMT Protocols
NSH 893	Phase II Trial Evaluating the Safety and Efficacy of Rituximab as Primary Treatment for Extensive Chronic Graft Versus Host Disease
NSH 894	A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma; BMT CTN 0702
NSH 900	BMT CTN 0804/CALGB 100701 Phase II Study of Reduced-Intensity Allogeneic Stem Cell Transplant for High-Risk Chronic Lymphocytic Leukemia (CLL) (available now through CTN)
NSH 911	A Phase II Trial of Post-Transplant Cyclophosphamide and Sirolimus for Graft-Versus-Host Disease (GVHD) Prophylaxis Following Reduced Intensity Allogeneic Hematopoietic Stem Cell Transplantation
NSH 916	BMT CTN 0803 High Dose Chemotherapy with Autologous Stem Cell Rescue for Aggressive B Cell Lymphoma and Hodgkin Lymphoma in HIV-infected Patients
NSH 922	A Phase II Trial of Total Body Irradiation-Based Myeloablative Conditioning and Transplantation of Partially HLA-Mismatched Peripheral Blood Stem Cells for Patients with Hematologic Malignancies
NSH 927	Defibrotide for Patients With Hepatic VOD: A Treatment IND Study
NSH 928	BMT CTN 0901A Randomized, Multi-Center, Phase III Study Comparing Myeloablative to Reduced Intensity Conditioning Transplants in Patients with Myelodysplastic Syndrome or Acute Myeloid Leukemia
NSH 936	BMT CTN 0301 Fludarabine-based Conditioning for Allogeneic Marrow Transplantation From HLA-compatible Unrelated Donors in Severe Aplastic Anemia
NSH 959	BMT CTN 0903 Allogeneic Hematopoietic Cell Transplant for Hematological Cancers and Myelodysplastic Syndromes in HIV-Infected Individuals
NSH 971	BMT CTN 0801 Phase II/III Randomized, Multi-Center Trial comparing Sirolimus plus prednisone vs Sirolimus/ Calcineurin Inhibitor plus prednisone in the treatment of chronic graft-versus-host disease.
NSH 988	MT CTN 1101 Multi-Center, Phase III, Randomized Trial of Reduced Intensity Conditioning (RIC) and Transplantation of Double Unrelated Umbilical Cord Blood versus HLA-Haploidentical Related Donor Bone Marrow for Patients with Hematologic Malignancies
NSH 955	A Multicenter safety study of unlicensed, investigational cryopreserved cord blood units (CBUs) manufactured by the National Cord Blood Program (NCBP) and provided for unrelated hematopoietic stem cell transplantation of pediatric and adult patients.
	NSH IRB- Leukemia/Lymphoma
NSH 898	A Randomized Phase III Study of Elacytarabine vs. Investigator's Choice in Patients with Late Stage Acute Myeloid Leukemia
NSH 923	A Phase III Randomized-Study of Oral Sapacitabine in Elderly Patients with Newly Diagnosed AML.
NSH 941	Randomized Phase II Trial of timed Sequential Therapy (TST) with Alvocidib (Flavopiridol), ara-C and mitoxantrone (FLAM) vs. "7+3" for Adults age 70 and Under with Newly Diagnosed AML
NSH 952	A Randomized, Multicenter Study Comparing Pixantrone + Rituximab with Gemcitabine + Rituximab in Patients with Aggressive B-Cell Non-Hodgkin Lymphoma who have relapsed after therapy with CHOP-R or an equivalent regimen and are ineligible for stem cell transplant
	NSH IRB-Supportive Care
NSH 721	NMDP Recipient Consent for Participation in Registry, Research Database, and Research Sample Repository
NSH 888	The Impact of Hematopoietic Stem Cell Transplantation on Primary Caregiver Level of Burden and Distress
NSH 909	A Prospective Assessment of the Diagnostic Utility of Emerging Laboratory Assessments Used in Conjunction with Fiberoptic Bronchoscopy (FOB) in Hematopoietic Stem Cell Transplant (HSCT) and Leukemia Patients with Acute Respiratory Symptoms and Pulmonary Infiltrates
NSH 940	A unique schedule of palonosetron, ondansetron, and dexamethasone for the prevention of delayed nausea and vomiting in patients receiving moderately emetogenic myeloablative chemotherapy
NSH 943	A multicenter access and distribution protocol for unlicensed cryopreserved cord blood units (CBUs) for transplantation in pediatric and adult patients with hematologic malignancies and other indications

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 BMT Program at Northside Hospital is a collaborative effort between the Blood and Marrow Transplant Group of Georgia and Northside Hospital. 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. The NSH-BMT Program also has received the prestigious designation of Core Clinical Center for the Blood and Marrow Transplant Clinical Trials Network (BMT-CTN), a designation accompanied by a research grant awarded by the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI). 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• Advancing Transfusion and Cellular Therapies Worldwide (AABB) • Food and Drug Administration (FDA)

Mission Statement

The NSH-BMT Program is committed to being the premier clinical transplant program in Georgia and the Southeast, providing outstanding state-of-the-art care for patients with leukemia and/or undergoing marrow and stem cell transplantation.

The NSH-BMT 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

To refer a patient, please call 404-255-1930.

The NSH-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 therapists.

Physicians at BMTGA:

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

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

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

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

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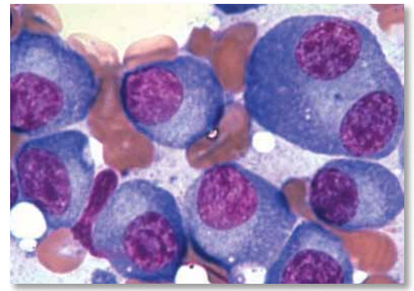
The Blood and Marrow Transplant Program at Northside Hospital News



Randomized Trials Address the Role of Maintenance Lenolidamide in Myeloma

by Asad Bashey, MD

The life expectancy of newly diagnosed patients with multiple myeloma has improved significantly in recent years partly as a result of the use of highly active biological therapy and high-dose chemotherapy with autologous stem cell transplantation. However, myeloma is still considered incurable in almost all patients and relapse of malignancy is common even following contemporary induction regimens. The accepted modern paradigm for treatment of patients who are under 70 years old and free of severe co-morbidities is the use of 4-6 cycles of induction therapy with a combination based on biologic agents followed by consolidation with high-dose chemotherapy and autologous stem cell transplantation. Conventionally, patients have enjoyed a 'holiday' from anti-myeloma treatment following the autologous transplant. Although many patients achieve a prolonged remission following this approach, others relapse earlier. Although conceptually attractive, the role of further consolidation or maintenance therapy after the autologous transplant given to prolong remission duration has been unclear. Agents assessed in previous trials of maintenance therapy have included alfa-interferon, corticosteroids, thalidomide and bortezomib. However, none of these agents have proved widely successful in this setting because of limited efficacy, problematic toxicity associated with long-term usage or difficulties associated with prolonged parenteral administration.

Lenalidomide is perhaps the most convenient of the currently available agents in this context because of its oral administration, manageable toxicity profile (especially the lack of associated severe peripheral neuropathy) and its robust activity against myeloma as a single agent. Three randomized Phase III trials

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assessing the role of lenalidomide as maintenance therapy have recently been published in the New England Journal of Medicine. Two of these trials studied the efficacy of prolonged low-dose lenalidomide as maintenance/consolidation therapy following autologous transplantation in the up-front therapy of multiple myeloma.

McCarthy et. al[1] reported on a phase III randomized trial performed in the United States and led by the Cancer and Leukemia Group B. The investigators randomly assigned 460 patients who were younger than 71 years of age and had stable disease or a marginal, partial, or complete response 100 days after undergoing stem-cell transplantation to lenalidomide or placebo, which was administered on a continuous schedule until disease progression. The starting dose of lenalidomide was 10 mg per day (range, 5 to 15). The study was unblinded when an interim analysis revealed that 20% of patients on lenalidomide versus 44 % of patients on placebo ($p < 0.001$) treatment died or had progressive disease. Eighty-six of 128 patients receiving placebo who had not yet progressed crossed over to lenalidomide maintenance. Median follow-up at the time of reporting was 34 months. Median time to progression post-transplant was significantly longer with lenalidomide maintenance (46 months vs. 27 months in the placebo group, $p < 0.001$). Despite the high crossover rate, more deaths were noted in the placebo arm (53, 23%) compared with the lenalidomide arm (35, 15%) ($P = 0.03$) leading to an overall survival benefit for the lenalidomide arm (three-year survival 88% vs. 80%, HR 0.62, 95% 0.40 to 0.95). Secondary cancers were noted in 18 (8%) and 6 (3%) of patients who received lenalidomide and placebo maintenance, respectively.

The trial by Attal et. al[2] was performed in France by the Intergroupe Francophone du Myelome (IFM). Most patients received two cycles of consolidation with lenalidomide 25 mg/day for 21 days out of 28 and the 614 patients enrolled were randomized (1:1) to maintenance lenolidomide (10-15 mg/d until disease progression). Median follow-up was 45 months from randomization. Median PFS was 41 months and 23 months with lenalidomide and placebo maintenance respectively ($p < 0.001$) with 4-year estimated probability of PFS being 43% vs. 22%, HR 0.5, $p < 0.000$). Unlike in the US trial, there was no significant difference in overall survival (4 year survival 73% vs. 75% respectively). Median event-free survival, including secondary cancers, was prolonged in the lenalidomide cohort at 40 months compared with 23 months in the placebo cohort ($p < 0.001$). By the time of study unblinding, 27% of lenalidomide arm and 15% of placebo arm had discontinued medication because of adverse effects. Thromboembolic events and hematological toxicity were higher in the lenolidamide arm. The incidence of secondary malignancies was 3.1 versus 1.2 per 100 patients-years in the lenalidomide and placebo maintenance cohorts, respectively ($p = 0.002$).

A third study has assessed the role of lenalidomide maintenance outside the context of autologous stem cell transplantation in patients older than 65 years. This trial, performed in Italy by Palumbo et. al[3] compared melphalan and prednisone (MP) versus MP lenalidomide (MPR) versus MPR plus lenalidomide maintenance therapy (MPR-R). Maintenance was administered at 10 mg 21 days out of 28 until disease progression or toxicity. At a median follow-up of 30 months, progression-free survival (PFS) was significantly prolonged after MPR-R (31 months) versus MPR (14 months, $p < 0.001$) or MP (13 months, $p < 0.001$). PFS benefit occurred in patients from 65 to 75 years old (and not in older patients). To date, there is no overall survival (OS) difference. Analysis has shown a 66% reduction in progressive disease after MPR-R treatment. The incidence of secondary cancers at three years was 7% in patients receiving MPR-R, 7% for those receiving MPR, and 3% for those receiving MP.

These three studies show that maintenance lenolidamide unequivocally prolongs PFS when used after induction therapy whether such therapy includes autologous transplantation or not. This benefit must be weighed against the inconvenience and expense of taking prolonged therapy and its associated toxicity. It also appears clear that the use of lenalidomide maintenance after alkylating agent therapy is associated with a statistically significant increase in second malignancies although the absolute number of such malignancies remains low, and recurrent myeloma remains a far greater hazard for these patients. Overall survival was only increased in one of the trials and it remains unclear whether an alternative strategy that involves treating at the earliest sign of disease-progression will also be less effective. However, these trials validate the use of lenalidomide in this context at least for high-risk patients and a full discussion of the benefits versus risks is justified in all patients.

1. McCarthy PL, Owzar K, Hofmeister CC, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366:1770-1781.
2. Atal M, Lauwers-Cances V, Marit G. et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366:1782-1791.
3. Palumbo A., Hajek R, Delforge M, et al. Continuous lenalidomide treatment for newly diagnosed multiple myeloma. N Engl J Med. 2012; 366:1759-1769.

Open for Enrollment NSH IRB 988: BMT CTN 1101 - Multi-Center, Phase III, Randomized Trial of Reduced Intensity Conditioning (RIC) and Transplantation of Double Unrelated Umbilical Cord Blood versus HLA-Haploidentical Related Donor Bone Marrow for Patients with Hematologic Malignancies

Study Highlights:

Both HLA- Haploidentical (partially matched related) donor and cord-blood units have been demonstrated to be effective and promising new sources of hematopoietic stem cells for patients who need an allogeneic hematopoietic stem cell transplant but have no suitable conventional donor. However, these approaches have never been compared to each other in a head-to-head randomized trial. BMT CTN 1101 is a newly opened national study that will determine which of these two approaches provides the best long term outcomes.
It is a multi-center, Phase III, randomized trial of reduced intensity conditioning followed by transplantation of two unrelated cord blood units (double umbilical cord-blood unit transplantation) versus HLA-haploidentical related bone marrow with post transplant cyclophosphamide (T-cell repletre haploidentical transplantation). Both groups will receive identical GVHD prophylaxis using, calcineurin inhibitor and MMF. Eligible malignancies are:

- Acute lymphoblastic leukemia/lymphoma, acute myelogenous leukemia, or Burkitt's lymphoma in remission.
- Lymphoma, including marginal zone lymphoma, follicular lymphoma, or chemotherapy-sensitive large-cell, Hodgkin, or mantle cell lymphoma.

Objectives:

The primary objective is to compare progression-free-survival at 2 years post-randomization between patients who receive unrelated double cord blood unit transplantation versus HLA-haploidentical related bone marrow transplantation.

Preparative Regimen: Randomized to dUCB or haplo-BMT:

	HAPLO Preparative Regimen
Day -6,-5	Fludarabine 30 mg/m2 IV over 30-60 minutes, then Cyclophosphamide 14.5 mg/kg IV over 1-2 hours*
Day -4→-2	Fludarabine 30 mg/m2 IV over 30-60 minutes
Day -1	TBI 200 cGy
Day 0	Non-T-cell depleted bone marrow
Days 3, 4	Cyclophopshamide 50 mg/kg IV Mesna 40 mg/kg IV*
Day 5	Begin tacrolimus (or cyclosporine), mycophenolate mofetil, and G-CSF
	dUCB Preparative Regimen
Day -6	Fludarabine 40 mg/m2 IV over 30-60 minutes, then Cyclophosphamide 50 mg/kg IV over 2 hours
Day -5→-2	Fludarabine 40 mg/m2 IV over 30-60 minutes
Day -3	Begin cyclosporine (or tacrolimus) and MMF
Day -1	TBI 200 cGY
Day 0	UCB Transplant
Day 1	Begin G-CSF

Donor Search:

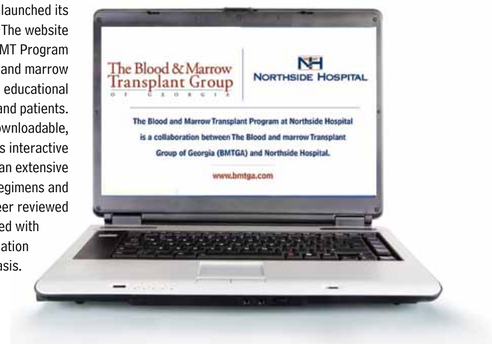
An unrelated donor search is not required for a patient to be eligible for this protocol if the clinical situation dictates an urgent transplant. Clinical urgency is defined as six to eight weeks from referral to transplant or a low-likelihood of finding a matched, unrelated donor. For more information, please call Stacey Brown, CCRP, Clinical Research & Data Supervisor at (404) 851-8238.

Additional Free Patient Lodging Options for NSH-BMT Patients

The Stovall Foundation, led by Ray and Martha Stovall, has donated another two fully-furnished apartments to the NSH-BMT Program. To date, the Stovall Foundation has donated a total of five apartments to the program and their donations have allowed patients and family members, who live fifty miles or greater from NSH, to be able to stay at a comfortable, safe and clean facility at no cost. Dr. Kent Holland, NSH-BMT FACT Medical Director, praises the Stovall Foundation's role in providing outstanding accommodations to those in need. "Through their generous efforts, The Stovall Foundation has continuously provided much needed free housing to NSH-BMT patients and their families," said Holland. "These apartments allow patients and family members to live comfortably in high quality living accommodations during transplant therapy while they are away from home."

BMT Launches New Website

On September 15th, BMTGA launched its new website, www.bmtga.com. The website showcases extensive NSH-BMT Program information, as well as blood and marrow transplant and leukemia educational information for physicians and patients. Educational PDF files are easily downloadable, and the new website also features interactive video clips, survival outcome data, an extensive list of BMT/leukemia protocols/regimens and BMT physician publications in peer reviewed journals. The site will be updated with new NSH-BMT Program information on a monthly basis.



Annual NSH Golf Tournament Raises Record Amount for NSH-BMT Program

On May 21, NSH-BMT's primary fundraiser, the 2012 Annual NSH Golf Tournament, was held at the Atlanta Athletic Club, and the event was a great success. The tournament, which brought in a record number of attendees and sponsors, raised more than a staggering $250,000 in generous donations. Money raised from the event goes towards financially assisting patients in need during the transplant process. We thank the NSH Foundation for their tireless efforts in organizing and coordinating this life-changing annual event.