The Blood and Marrow Transplant Program at Northside Hospital News

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SPRING 2012
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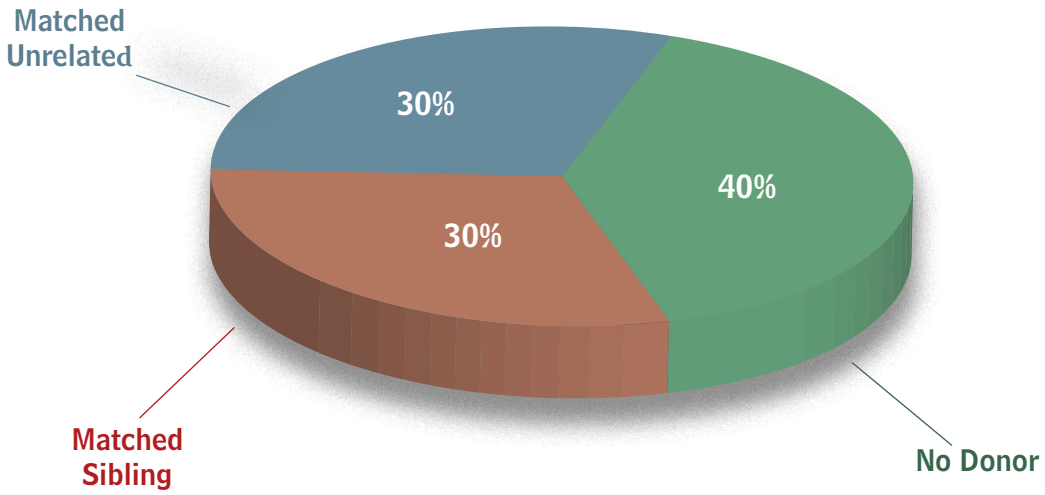
HLA-Haploidentical Relatives are Suitable Alternative Donors for Patients Lacking Conventional Donors for Allogeneic Hematopoietic Transplantation



Research from NSH-BMT Demonstrates that T-Cell Replete Allogeneic Transplants from Haploidentical Donors have Similar Outcomes to Transplants from Conventional Matched Sibling and Matched Unrelated Donors

Allogeneic hematopoietic cell transplant (allo-HCT) can cure several hematological malignancies that are incurable with standard therapies. Successful allo-HCT requires the availability of a suitably matched donor such as an HLA-identical sibling (MRD) or a 10 of 10 locus HLA-A, B, C and DRB1 matched unrelated donor (MUD). Unfortunately, many patients, especially those from minority and mixed ethnic backgrounds will lack such a donor. Cryopreserved umbilical cord blood (UCB) has been used as an alternative donor source for such patients. However, UCB units often contain insufficient cells for an adult recipient and UCB transplants can be associated with slow immunological recovery in adult recipients with associated prolonged risk of opportunistic infections and other post-transplant complications. Almost all patients who need an allo-HCT have a first degree relative with whom they share a HLA-haplotype. Un-manipulated allo-HCT from such haploidentical donors have resulted in unacceptable rates of graft rejection and severe graft-versus-host disease (GVHD). Thus a conventional approach to allo-HCT from haploidentical donors in centers such as Perugia, Italy has involved stringent depletion of T-cells from the graft to prevent GVHD and very intense preparative regimens to prevent graft-rejection. Although such transplants are feasible, they are associated with high-rates of

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regimen related toxicity and very slow immunological recovery with associated high rates of treatment related mortality1,2.

Recently an alternative approach to allo-HCT from haploidentical donors has been developed which uses no ex-vivo T-cell depletion and instead uses post-transplant cyclophosphamide (Haplo-ptCy) to relatively specifically eliminate alloreactive T-cells responsible for graft-rejection and GVHD, while preserving other T-cells that are important for immunologic recovery3,4. Haplo-ptCy have been shown to result in low rates of GVHD, infections and treatment related mortality in single and multicenter trials including a parallel phase-II comparison to UCB transplantation conducted by the Blood and Marrow Transplantation Clinical Trials Network (BMT-CTN)5. However, Haplo-ptCy has not been formally compared to allo-HCT performed using conventional MRD or MUD donors.

In a paper presented at an oral session at the 53rd annual meeting of the American Society of Hematology meeting (December 2011, San Diego, CA, Abstract 833; Blood vol 118 (21) p380) researchers from NSH-BMT compared outcomes following 53 consecutive Haplo-ptCy to 117 consecutive allo-HCT from MRD and 101 from MUD respectively. All transplants were performed contemporaneously at NSH-BMT using identical supportive care measures. The patients undergoing allo-HCT from the three types of donor were well matched with respect to age, gender, diagnosis, risk-profile of malignancy and co-morbidities. Haplo-ptCy patients were more likely to receive bone marrow rather than peripheral blood stem cell grafts and more likely to receive reduced intensity versus myeloablative preparative conditioning for transplant. A Cox proportional hazards analysis was conducted and outcome measures were adjusted for any difference in confounding variables between the three groups. The results demonstrated that patients who underwent Haplo-ptCy had similar overall and disease-free survival to patients transplanted from MRD and MUD respectively (Fig 1A,B). Cumulative incidences of non-relapse-mortality and relapse of malignancy (Fig 1C, D) were also not significantly different between the three groups. Rates and severity of acute GVHD were similar but cumulative incidence of extensive and severe chronic GVHD were lower in Haplo-ptCy patients.

This study is the first to compare a large number of allo-HCT performed using Haplo-ptCy to contemporaneous allo-HCT performed from MRD and MUD at the same center. It shows that Haplo-ptCy produces similar outcomes to transplants performed from conventional donors. Thus Haplo-ptCY represents a valid standard of care in patients who lack a conventional donor.

1. Aversa F, Terenzi A, Tabilio A, et al: Full haplotype-mismatched hematopoietic stem-cell transplantation: a phase II study in patients with acute leukemia at high risk of relapse. J Clin Oncol 23:3447-54, 2005

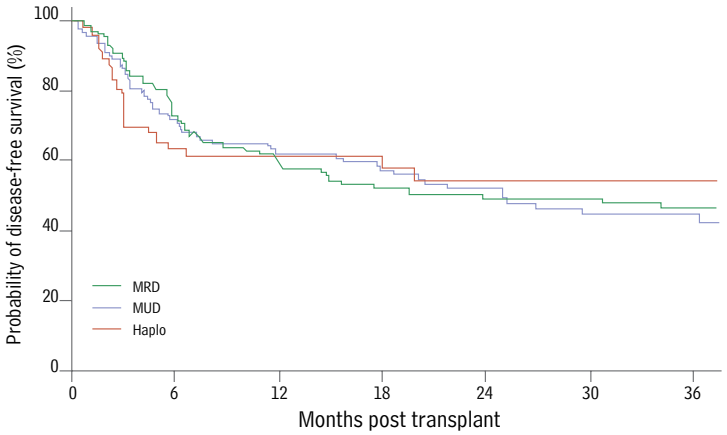
2. Ciceri F, Labopin M, Aversa F, et al: A survey of fully haploidentical hematopoietic stem cell transplantation in adults with high-risk acute leukemia: a risk factor analysis of outcomes for patients in remission at transplantation. Blood 112:3574-81, 2008

3. Kasamon YL, Luznik L, Leffell MS, et al: Nonmyeloablative HLA-haploidentical bone marrow transplantation with high-dose posttransplantation cyclophosphamide: effect of HLA disparity on outcome. Biol Blood Marrow Transplant 16:482-9, 2010

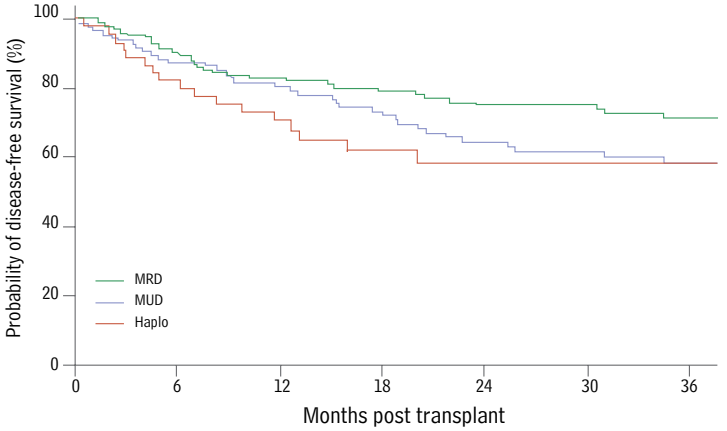
4. Luznik L, O'Donnell PV, Symons HJ, et al: HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. Biol Blood Marrow Transplant 14:641-50, 2008

5. Brunstein CG, Fuchs EJ, Carter SL, et al: 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 118:282-8, 2011

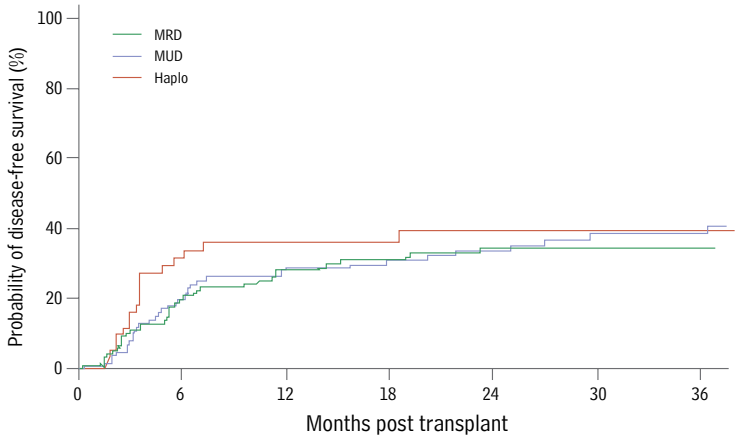
ADJUSTED DISEASE-FREE SURVIVAL



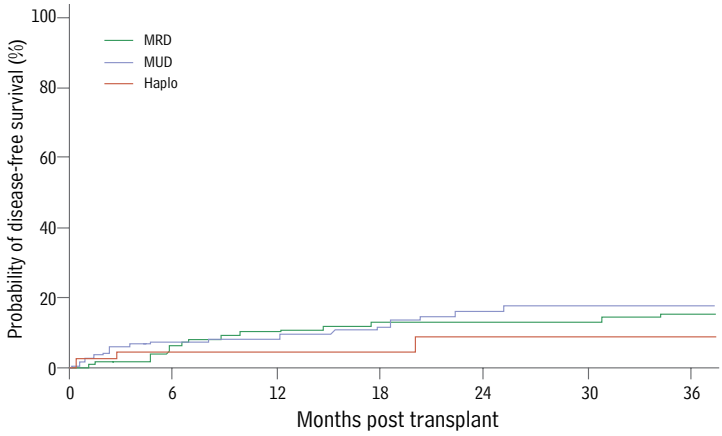
ADJUSTED OVERALL SURVIVAL



CUMULATIVE INCIDENCE OF RELAPSE MALIGNANCIES



CUMULATIVE INCIDENCE OF NON-RELAPSE MORTALITY



Highlights from the BMT InfoNet's Fourth National Survivorship Symposium

The NSH-BMT Team is committed to transitioning patients from sickness to wellness. As part of this commitment, the NSH-BMT Program was a Gold Level sponsor for the two-day BMT InfoNet Survivorship Symposium in Atlanta, Ga. The symposium brought together key leaders and speakers to focus on seeing patients through the continuum of care.

More than 350 patients and family members received critical information from experts in the field of blood and marrow transplantation and psychosocial support. Most importantly, the symposium provided hope for patients and family members.

Symposium Highlights included:

- 30 different workshops & 42 expert presenters, including many NSH-BMT staff members
- Educational & support topics ranged from how to detect and manage physical complications arising after transplant to coping with psychological changes
- Meet the Expert panel featured transplant directors from across the Southeast, including Dr. H. Kent Holland, FACT Program Director for NSH-BMT

NSH-BMT Hosts Kaiser Educational Summit

The NSH-BMT Team is committed to providing cutting-edge disease specific treatment for hematological malignancies. In February, 22 of Kaiser Permanente's Atlanta hematology/oncology and national BMT team members participated in a NSH-BMT Educational Summit. BMT physicians and staff members provided the latest diagnostic and treatment advances in acute/chronic leukemia, hodgkin's disease, non-hodgkins lymphoma, multiple myeloma and solid tumors. This effort is part of the NSH-BMT Program's commitment to continuing education of partner physicians and payor groups. The summit forged stronger partnerships among Atlanta based Kaiser hematology/oncology physicians and the national Kaiser Transplant Network while promoting improved patient care.

NSH-Leukemia Program Opens New Acute Leukemia-Lymphoma Trials

New cutting edge clinical research trials are open for patients who have a newly diagnosed/refractory acute leukemia or a relapsed Aggressive B-Cell Non-Hodgkin Lymphoma. NSH-BMT's commitment to advancing the field of leukemia/lymphoma therapies is reflected in the program's dedicated interdisciplinary leukemia team, state-of-the-art treatment facilities and ability to get access to new leukemia/lymphoma clinical research trials. If you have a patient who may be eligible for one of these trials, or if you have a question regarding eligibility, please call Stacey Brown at 404-851-8238.

	NSH Acute Leukemia & Lymphoma Protocols
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 Patient 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

Patient Support: NSH-BMT/Leukemia Coordinator's Office

The coordinator's office plays a key role in organizing and coordinating new patient referrals (NPC), Pre/Post BMT/leukemia schedules and follow-up evaluation studies. The coordinator organizes details of the procedure, communicates to all parties, works through issues and problems and most importantly, ensures each patient is prepared to undergo BMT/leukemia therapy. NSH-BMT is fortunate to have 10 highly trained full time BMT/Leukemia Program coordinators.

Job functions of BMT/Leukemia Coordinators:

- Contacting the NPC, scheduling appointments and obtaining prior medical records
- Continuous communication with patient/referring MD office/ NSH-BMT physician team
- Scheduling Pre/Post BMT evaluation studies
- Obtaining/reviewing required pre-post BMT testing results
- Participating in clinical transplant program's quality improvement plan/initiatives

NSH-BMT Team Present at OptumEducation Spotlight

The NSH-BMT Program and Piedmont Hospital's Transplant Institute co-hosted the OptumEducation Spotlight Event at Georgia Aquarium. The NSH-BMT Program was the only center in the Southeast to be asked to host an Optum Spotlight educational event.

Discussions and lectures included BMT and solid organ topics. BMTGA physicians/outpatient BMT team lectures included the following:

- Auto vs. Allo: Which is best for which disease?
- Donor Matching: Is a half match better than a full match?
- GVHD: Friend or foe?
- Allogeneic Transplant: No longer a risky Procedure!
- A journey through transplant
- HSCT: Does it make a difference where you go?

At the conclusion of the BMT lectures, a reception in the Artic Beluga Whale Room brought together event participants to enjoy cocktails, hors d'oeuvres from Wolfgang Puck Catering and aquarium events.

	NSH IRB approved BMT Protocols For protocol eligibility questions, please call Stacey Brown at 404-851-8238.
NSH 721	NMDP Recipient Consent for Participation in Registry, Research Database, and Research Sample Repository
NSH 886	A Randomized, double-blind, placebo-controlled Phase III study of SGN-35 (brentuximab vedotin) and BSC versus placebo and BSC in the treatment of patients at high risk for residual HL following ASCT
NSH 888	The Impact of Hematopoietic Stem Cell Transplantation on Primary Caregiver Level of Burden and Distress
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)
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 or Lymphoma Patients with Fever and/or Acute Respiratory Symptoms and Pulmonary Infiltrates
NSH 911	A Phase II Trial of Post-Transplant Cyclophosphamide for Graft Versus Host Disease (GVHD) Prophylaxis Following Reduced Intensity Unrelated Donor Allogeneic Peripheral Blood 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 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
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.

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.

NCI COMMUNITY CANCER CENTERS PROGRAM

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

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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