NORTHSIDE HOSPITAL CANCER INSTITUTE
BLOOD & MARROW TRANSPLANT PROGRAM

Transplant and Cellular Immunotherapy NEWS

NORTHSIDE HOSPITAL CANCER INSTITUTE
IMMUNOTHERAPY PROGRAM

FALL 2019 ISSUE

IN THIS ISSUE:

National Outcomes Database Reports Extraordinary Ten-Year Record of Continuous Superior-Than-Expected Survival Outcomes for the Northside BMT Program

Northside is the Only BMT Program in Georgia to Report Superior Outcomes in the Current Report

By: Asad Bashey, MD, PhD

Latest data provided by The Centers for International Blood and Marrow Transplant Research (CIBMTR) show that the Blood and Marrow Transplant Program at Northside Hospital (NH-BMT) has achieved allogeneic transplant survival outcomes for 10 consecutive years that are significantly better than would be expected, given the risk profile of patients transplanted at our center. NH-BMT is one of only two BMT Programs in the entire United States to achieve this feat. Furthermore, for the last reported period, NH-BMT is the only center in Georgia, Alabama or the Carolinas that has reported outcomes that are significantly better than expected.

The CIBMTR is the premier organization tasked with reporting outcomes worldwide for hematopoietic cell transplantation and cellular therapy. The CIBMTR is funded and tasked by the Federal Government of the United States to provide annual reports on survival outcomes from all active BMT programs in the United States through its Stem Cell Transplant Outcomes Database (SCTOD). Reporting center-specific survival rates is a requirement of the Stem Cell Therapeutic and Research Act of 2005. The annual reports describe the key metric of one-year survival following allogeneic transplantation for all first allogeneic transplants performed by each transplant program. These outcome data are compared to the risk-adjusted, one-year survival rate calculated for each BMT program (survival that would be expected for each center, considering the risk factors of the actual patients being transplanted). Results from each program are then reported as equal to expected, superior to expected or inferior to expected. In order for a program's performance to be designated superior to expected, the difference between actual and expected outcomes and the number of patients transplanted needs to be sufficiently large for the results to be very unlikely to be explained by chance upon statistical analysis.

All 177 active BMT centers in the United States are required by federal law to report their data to the CIBMTR for compilation into the SCTOD. The analysis considers all patient, disease and transplant-related factors known to significantly affect outcomes. Therefore, the results and their variation from expectation cannot be explained by patient selection and truly represent a clear measure of the quality of care provided at the transplant center.

The Revised Final 2018 Transplant Center-Specific Survival Report was made available by the CIBMTR on February 8th, 2019. The current analysis includes patients undergoing allogeneic transplants during the three-year time interval from January 1, 2014 to December 31, 2016, with follow-up through December 31, 2017. Each center is designated as "overperforming" (significantly superior than predicted), "predicted" (average) or "underperforming" (significantly inferior than predicted) based upon whether its survival outcome is above, within or below the 95% confidence intervals respective of the average survival prediction, based upon the risk profile of patients transplanted at that center.

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Current Results Continue to Demonstrate Exceptional and Superior Outcomes of the Northside BMT Program

The latest annual report reveals:

- Only 13 of 177 BMT Programs nationwide were overperforming (7.3%).
- 25 of the 177 BMT Programs were underperforming (14%).
- 139 of 177 BMT Programs performed as predicted (78.5%).
- NH-BMT was the only program in the state of Georgia to be an overperforming center.
- For the latest reporting period, NH-BMT's one-year survival rate was 79.4% while its predicted one-year survival rate based on the risk profile of the patients it transplanted was 67.5%.
- NH-BMT is one of only two centers of 177 in the entire United States to have an unbroken record of superior to expected survival outcomes for the last 10 years. The only other center in the nation to achieve this feat is the BMT Program City of Hope Medical Center in California.

The fact that only approximately one in ninety transplant centers have had such consistently outperforming survival outcomes highlights the truly exceptional nature of this achievement and places NH-BMT among the two top BMT Programs for patient survival nationwide. It also emphasizes that the superior survival outcomes at NH-BMT are not a temporary statistical anomaly, but represent the extraordinary quality of care provided by NH-BMT year-upon-year. The anticipated versus actual survival outcomes at NH-BMT over the last ten years are illustrated in Figure 1.

Approaches to BMT That Underlie the Superior Outcomes Seen at NH-BMT

Numerous structural and technical differences between NH-BMT and other transplant programs underlie the exceptional outcomes seen at NH-BMT. Among these are:

1) NH-BMT is currently the largest allogeneic BMT center in Georgia and one of the largest in the southeastern United States.

2) All transplant physicians are full-time clinicians with a primary interest in BMT (unlike other programs where many physicians whose main clinical interest is not BMT) or are primarily laboratory-based researchers, help cover the BMT service.

3) The only physicians involved in caring for BMT patients at NH-BMT are highly experienced and fully trained attending physicians. In contrast, residents and fellows routinely care for transplant patients in other centers.

4) Attending BMT physicians take first call during nights and weekends at NH-BMT. This way patients calling the program can have immediate access to an experienced attending BMT physician, unlike another program where calls are filtered through physicians-in-training or physician extenders.

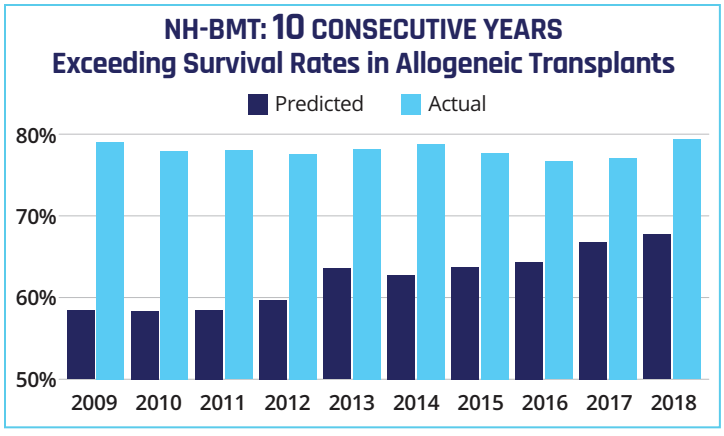
5) NH-BMT has invested extensively in resources and facilities to allow patients undergoing allogeneic BMT to remain in the outpatient setting for all or most of their transplant care. In contrast, most other programs require their patients to be confined to inpatient rooms during this time. Outpatient care for allogeneic transplants has been shown to result in superior outcomes. This is partly because outpatients tend to be more physically active and are less exposed to hospital-acquired infections.

6) NH-BMT has a highly organized and proactive Quality Improvement Program, which regularly analyzes outcomes and outcome parameters, and then institutes measures to improve them. It has served as a model for other transplant centers. The Quality Program is one reason why NH-BMT has passed six consecutive tri-annual inspections by the Foundation for Accreditation of Cellular Therapy (FACT) without any detected deficiencies, which is extremely rare.

7) NH-BMT employs seven full-time pharmacists who are devoted to the BMT Program. This is among the highest ratio of pharmacists to patients of any BMT program nationwide. Among their many responsibilities the pharmacists of NH-BMT monitor medications of the transplant patients to ensure compliance and avert medication interactions.

We are thankful to our many referring physicians, our dedicated staff and the courage and determination of our patients for making these extraordinary results possible.

Figure 1.



Pictured above: Melissa Henson, RN, Manager of Cellular Therapy and Leukemia Program and Ashlee Holbein, RN, FACT/QI Coordinator

For the Sixth Consecutive Foundation for the Accreditation of Cellular Therapy (FACT) Re-inspection Cycle, the NH-BMT Clinical Transplant Program Receives a Perfect Score

In November 2018, the NH clinical BMT team underwent a FACT inspection, which occurs every three years. It was also the first year FACT required transplant centers to undergo Immune Effector Cells (IEC) accreditation. The new IEC policies apply to immune effector cells used to modulate an immune response for therapeutic intent, such as dendritic cells, natural killer cells, T cells and B cells. IEC includes chimeric antigen receptor T cells (CAR-T cells) and therapeutic vaccines.

The inspection team complimented NH-BMT's physician oversight, trained team members, organizational structure, superior survival outcomes and programmatic commitment to excellent patient care and awarded the program a perfect FACT Inspection score. We want to congratulate our NH-BMT clinical transplant team members for this distinguished honor.

Beth Wilson and Unrelated Donor Meet in Germany

Pictured Above: Alina Theine (donor) and Beth Wilson (NH-BMT unrelated donor recipient)

Beth Wilson's husband surprised her for her October 2018 birthday with a March 2019 trip to Germany. Unbeknownst to Beth, her unrelated donor, Alina Theine, was waiting at the train station when she arrived in Germany. The German donor registry, DKMS Deutschland that helped facilitate Alina's donor collection with the NH-BMT Program, was at the train station filming their first meeting. Beth, her husband and Alina then traveled to the medical clinic, Cellex, to meet with medical staff who participated in Alina's donation.

Germany's national news broadcasted Beth and Alina's meeting. Since their story aired, over 300 potential donors have signed up to the DKMS donor registry. Beth and Alina also told their story to three classes in two different schools and emphasized the importance of donating blood or marrow. One of the schools they visited had a student who matched a patient and had begun the donation process.

If you are interested in becoming a donor, please visit https://bethematch.org/support-the-cause/donate-bone-marrow/

Hoa Le, RN, NH-BMT/Leukemia/Immunotherapy Unit Nurse, Honored at the Atlanta Journal-Constitution (AJC) Nursing Excellence Awards

We would like to congratulate Hoa Le, RN, for being selected by the AJC as one of the top 10 nurses in Georgia at the 14th annual Celebrating Nurses Awards. There were over 800 nominations. Hoa's commitment to providing outstanding patient care has helped the NH-BMT/Leukemia/Immunotherapy program to continue to have excellent survival rates and exceptional patient satisfaction.

CAR T-cell Clinical Research Trials Available for Multiple Myeloma, Non-Hodgkin's Lymphoma, Small Lymphocytic Lymphoma and Chronic Lymphocytic Leukemia

Please contact Stacey Brown, NH-BMT/Leukemia/Immunotherapy Research Manager, at 404-780-7965 or stacey.brown@northside.com, to discuss study logistics and eligibility/exclusion criteria.

Disease	Trial Number	Name of Trial	Drug & NCT Identifier
CLL/Small Lymphocytic Lymphoma	**NSH1226**	An Open-Label, Phase 1 Safety and Phase 2 Randomized Study of JCAR017 in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma	JCAR017 NCT03331198
Multiple Myeloma	**NSH1216**	A Phase 3, Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of bb2121 versus Standard Triplet Regimens in Subjects with Relapsed and Refractory Multiple Myeloma (rrMM) (KarMMa-3)	bb2121 NCT03651128
NHL	**NSH1170**	A Phase 1, Multicenter, Open-Label Study of JCAR017, CD19-Targeted Chimeric Antigen Receptor (CAR) T-Cells, in Relapsed and Refractory (R/R) B-Cell Non-Hodgkin Lymphoma	JCAR017 NCT02631044
	NSH1207	A Global Randomized, Multicenter Phase 3 Trial to Compare the Efficacy and Safety of JCAR017 to Standard of Care in Adult Subjects with High-Risk, Transplant-Eligible Relapsed or Refractory Aggressive B-Cell Non-Hodgkin Lymphomas (TRANSFORM)	JCAR017 NCT03575351
	NSH1230	A Phase 2 Study of Lisocabtagene Maraleucel (JCAR017) as Second-Line Therapy in Adult Patients with Aggressive B-Cell NHL	JCAR017 NCT03483103

NSH1226

Inclusion Criteria
- Age ≥ 18
- ECOG PS ≤ 1
- CLL with clinically measurable disease
- SLL with clinically measurable disease

Exclusion Criteria
- Known active CNS disease
- History of another primary malignancy <2 yrs
- Richter's transformation

NSH1216

Inclusion Criteria
- Age ≥ 18
- ECOG PS 0 or 1
- Received 2 - 4 prior MM regimens
- Received prior treatment with daratumumab, a proteasome inhibitor and an immunomodulatory compound containing regimen for at least 2 consecutive cycles
- Refractory to the last treatment regimen
- Achieved at least a minimal response to at least 1 prior treatment regimen
- Has received and failed Bruton tyrosine kinase inhibitor (BTKi) treatment or is ineligible for BTKi treatment.

Exclusion Criteria
- Active or history of plasma cell leukemia, WM, POEMS syndrome, or amyloidosis
- COPD with FEV1 50% of predicted normal
- Therapy-based therapeutic for cancer, investigational cellular therapy for cancer, or BCMA targeted therapy
- Received an autologous stem cell transplant within 12 wks prior to randomization

NSH1170

Inclusion Criteria
- Age ≥ 18 years
- ECOG PS between 0 and 1
- Relapsed or refractory B-cell NHL or Mantle Cell Lymphoma (MCL)
- Previous treatment of at least 2 lines of therapy or 1 line in MCL or after auto HSCT
- Archived tumor biopsy tissue available from the last relapse and corresponding pathology report available for disease confirmation, and willing to undergo pre- and post-treatment biopsy if at least one tumor-involved site is deemed accessible at time of screening

Exclusion Criteria
- CNS only involvement with malignancy-secondary CNS involvement are allowed on study
- Active acute or chronic GVHD
- Prior malignancy <2 yrs
- Active hepatitis B, hepatitis C, or HIV

NSH1207

Inclusion Criteria
- Age ≥18 and ≤ 75 at time of consent
- ECOG PS ≤ 1
- Relapsed or refractory B-cell NHL
- Refractory (SD,PD,PR, or CR with relapse before 3 months) or relapsed (CR with relapse on or after 3 months) within 12 months from CD20 antibody and anthracycline containing first line therapy
- Must have PET positive lesion(s) at screening
- Enough tumor material must be available for confirmatory by central pathology
- Secondary CNS involvement is acceptable

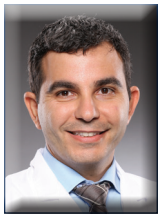
Exclusion Criteria
- Not eligible for HSCT
- Previous CD-19 targeted therapy
- Planned allo HSCT
- Prior malignancy resolved < 2yrs
- Treatment with prior gene therapy
- History/active hepatitis B, hepatitis C or HIV

NSH1230

Inclusion Criteria
- Age ≥ 18
- ECOG PS 0-2
- Diagnosis:
  - DLBCL NOS or transformed from follicular lymphoma
  - High grade B-Cell lymphoma with MYC and BCL and/or BCL6 rearrangements with DLBCL histology (double/triple hit lymphoma [DHL/THL])
  - Follicular lymphoma Grade 3B
- Previous treatment must include single line of chemoimmunotherapy containing an anthracycline and a CD20 targeted agent
- Subjects must be deemed ineligible for both high-dose chemotherapy and HSCT while also having adequate organ function for CAR T-cell treatment

Exclusion Criteria
- Subjects with central nervous system (CNS)-only involvement by malignancy (subjects with secondary CNS involvement are allowed on study)
- Previous CD-19 targeted therapy and or prior HSCT

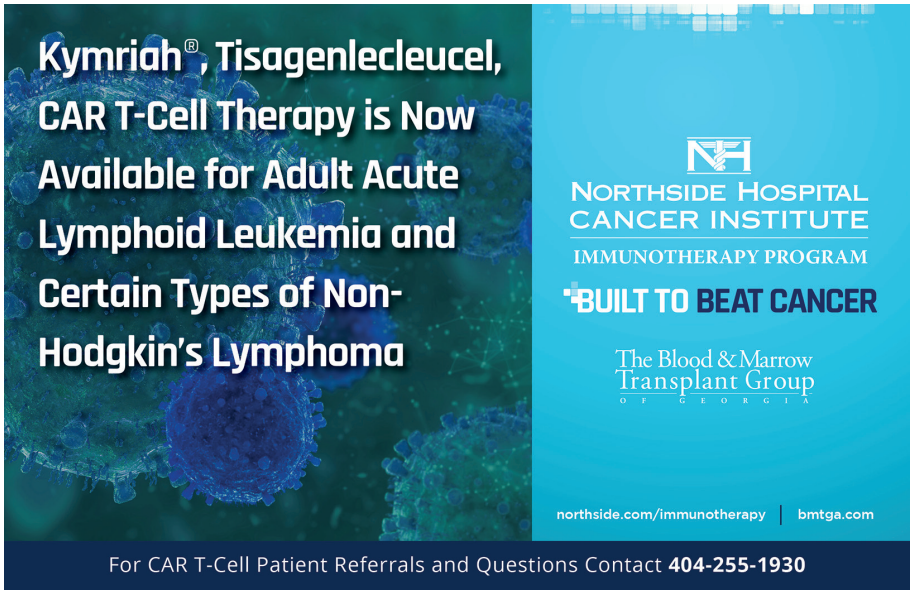
Dr. Melhem Solh Presents at Pat's Myeloma Survival School 2019



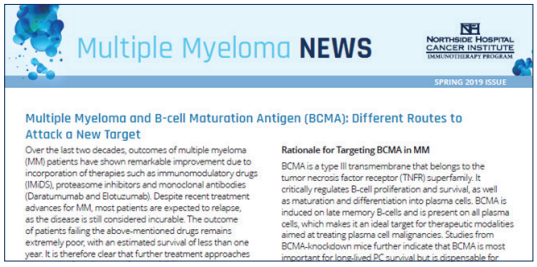
On May 18-19, 2019 the Leukemia Lymphoma Society and their best advice foundation sponsored a comprehensive educational event for multiple myeloma patients, family members and caregivers. NH's Dr. Solh presented on new developments in immunotherapy treatments and explained how immunotherapy works differently than standard myeloma drug therapies. To learn more about the NH-Immunotherapy program, please visit bmtga.com/immunotherapy-program-at-northside/.

LEUKEMIA & LYMPHOMA SOCIETY®

tba their best advice foundation



NH-Immunotherapy Program Program Publishes First Multiple Myeloma Newsletter



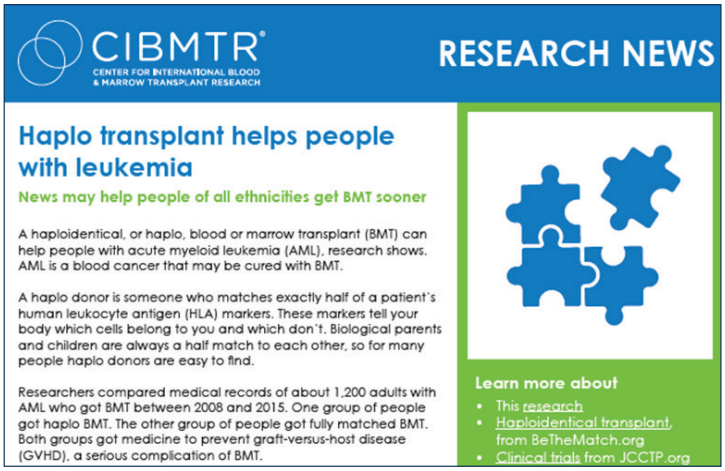
Please visit http://www.bmtga.com/wp-content/uploads/2019/04/MM-Newsletter-Spring-2019-v2.pdf to read the entire Newsletter.

Center for International Blood and Marrow Transplant Research (CIBMTR) Highlights Program's Clinical Research Study, *Outcomes of Haploidentical vs Matched Sibling Transplantation for Acute Myeloid Leukemia in First Complete Remission*

As a pioneer in the field of haploidential transplantation, we are honored to have CIBMTR share with the public our groundbreaking clinical research trial results. This study was one of three selected during the third quarter of 2019 by the Consumer Advocacy Committee.

To read this article, please visit the following links:

- Twitter (https://twitter.com/CIBMTR)
- Facebook (https://facebook.com/theCIBMTR/)
- CIBMTR Study Summaries for Patients page (https://www.cibmtr.org/Reference Center/Patient/PatientSummaries/Pages/index.aspx)



Open Trial List

Disease	Trial Number	Name of Trial	Drug & Link to www.clinicaltrials.gov
Immunotherapy	NSH1150	Phase 2 Trial of Lymphodepletion and Anti-PD-1 Blockade to Reduce Relapse in High-Risk AML Patients Who Are Not Eligible for Allogeneic Stem Cell Transplantation	Pembrolizumab NCT02771197
	C332	A Phase I Study of Ipilimumab in Combination with Decitabine in Relapsed or Refractory Myelodysplastic Syndrome/Acute Myeloid Leukemia	Ipilimumab NCT02890329
	NSH1224	A Phase I, Open Label Study to Evaluate the Safety, Pharmacokinetic, Pharmacodynamic and Clinical Activity of PF-06863135, A B-Cell Maturation Antigen (BCMA) – CD3 Bispecific Antibody, in Patients with Relapsed/Refractory Advanced Multiple Myeloma (MM)	PF-06863135 NCT03269136
	C378	A Phase I Trial of the Combination of Lenalidomide and Blinatumomab in Patients with Relapsed/Refractory NHL	Lenalidomide/ Blinatumomab NCT02568553
	C379	Randomized Phase 2 Study of CDX-1127 (Varlilumab) in Combination with Nivolumab in Patients with Relapsed or Refractory Aggressive B-Cell Lymphomas	CDZ-1127 Varlilumab NCT03038672
CAR T-cell: NHL	NSH1170	A Phase 1, Multicenter, Open-Label Study of JCAR017, CD19-Targeted Chimeric Antigen Receptor (CAR) T Cells, in Relapsed and Refractory (R/R) B-Cell Non-Hodgkin Lymphoma	JCAR017 NCT02631044
	NSH1207	A Global Randomized, Multicenter Phase 3 trial to Compare the Efficacy and Safety of JCAR017 to Standard of Care in Adult Subjects with High-Risk, Transplant-Eligible Relapsed or Refractory Aggressive B-Cell Non-Hodgkin Lymphomas (TRANSFORM)	JCAR017 NCT03575351
	NSH1230	A Phase 2 study of Lisocabtagene Maraleucel (JCAR017) as Second-Line Therapy in Adult Patients with Aggressive B-cell NHL	JCAR017 NCT03483103
CAR T-cell: CLL/Small Lymphocytic Lymphoma	NSH1226	An Open-Label, Phase 1 Safety and Phase 2 Randomized Study of JCAR017 in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma	JCAR017 NCT03331198
CAR T-cell: Multiple Myeloma	NSH1216	A Phase 3, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of bb2121 versus Standard Triplet Regimens in Subjects with Relapsed and Refractory Multiple Myeloma (rrMM) (KarMMa-3)	bb2121 NCT03651128
AML	NSH1164	A Phase 1 Multiple Dose Study to Evaluate the Safety and Tolerability of XmAb® 14045 in Patients With CD123-Expressing Hematologic Malignancies	XmAB® 14045 NCT02730312
	NSH1208	A Phase 1 Trial to Evaluate the Potential Impact of Renal Impairment on the Pharmacokinetics and Safety of CPX-351 (Daunorubicin and Cytarabine) Liposome for Injection Treatment in Adult Patients with Hematologic Malignancies	Vyxeos NCT03555955
	NSH1223	A Phase 1b Dose-escalation Study to Assess the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of PLX2853 in Subjects with Relapsed or Refractory Acute Myeloid Leukemia or High-risk Myelodysplastic Syndrome	Plexxikon NCT03787498

(continued on page 7)

Open Trial List *(continued)*

Disease	Trial Number	Name of Trial	Drug & Link to www.clinicaltrials.gov
Transplant	C373	BMT CTN 1702 Clinical Transplant-Related Long-Term Outcomes of Alternative Donor Allogeneic Transplantation	NCT03904134
	C369	BMT CTN 1703 A Randomized, Multicenter, Phase III Trial of Tacrolimus/Methotrexate versus Post-Transplant Cyclophosphamide/ Tacrolimus/ Mycophenolate Mofetil in Non-Myeloablative/ Reduced Intensity Conditioning Allogeneic Peripheral Blood Stem Cell Transplantation	NCT03959241
Multiple Myeloma	NSH1107	A Phase 2 Trial of High-Dose Bendamustine, Etoposide, Cytarabine, and Melphalan (BeEAM) in the Upfront Treatment of Multiple Myeloma	Bendamustine NCT02416206
Aplastic Anemia	NSH1158	A Study of T Cell Replete, HLA-Mismatched Bone Marrow Transplantation With Post-Transplant Cyclophosphamide as a Front-Line Therapy for Patients With Severe Aplastic Anemia Lacking HLA-Matched Related Donor	Fludarabine Cyclophos NCT02828592
Sickle Cell Anemia	NSH1184	Reduced Intensity Conditioning for Haploidentical Bone Marrow Transplantation in Patients with Symptomatic Sickle Cell Disease	NCT03263559
Post Transplant			
AML	NSH1182	BMT CTN 1506 Randomized Trial of FLT3 Inhibitor vs Placebo as Maintenance Therapy Post Allogeneic Transplant	Gilteritinib NCT02997202
Multiple Myeloma	C389	Phase III Study of Daratumumab/rHuPh20 (NSC-810307) Plus Lenalidomide or Lenalidomide as Post Autologous Stem Cell Transplant Maintenance Therapy in Patient with Multiple Myeloma (MM) using Minimal Residual Disease to Direct Therapy Duration (Dramatic Study).	Daratumumab/ rHuPh20 (NSC-810307) NCT04071457
Supportive Care/ Other	NSH721	NMDP Recipient Consent for Participation in Registry, Research Database, and Research Sample Repository	NCT00495300 (sample) NCT01166009 (database)
	NSH943	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	NCT01351545
	NSH995	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	NCT01656603
	C393	BMT CTN 1704 Composite Health Assessment Model for Older Adults: Applying Pre-Transplant Comorbidity, Geriatric Assessment, and Biomarkers to Predict Non-Relapse Mortality after Allogeneic Transplantation (CHARM)	NCT03992352

NH-BMT Presents at the Leukemia and Lymphoma Society's Annual Georgia Blood Cancer Conference

Over three hundred and fifty attendees participated in this free educational conference for patients, survivors and health care professionals. Dr. Melhem Solh presented an overview of state-of-the-art multiple myeloma treatments and Connie Sizemore, PharmD, Lead Clinical Pharmacy Specialist, spoke about Transplant Survivorship.

The Blood and Cancer Conference (BBC) is one of many programs developed by the Leukemia Lym-phoma Society (LLS) to meet the needs of people who deal with blood cancer everyday and for the people that care for them.

Blood & Marrow Transplant Group
at Northside Hospital
5670 Peachtree Dunwoody Road
Suite 1000
Atlanta, GA 30342

BMTGA Physicians

(L-R) Drs. H. Kent Holland, Asad Bashey,
Melhem Solh, Scott Solomon and Lawrence Morris

To make a referral, or to speak with a physician, please call (404) 255-1930.

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