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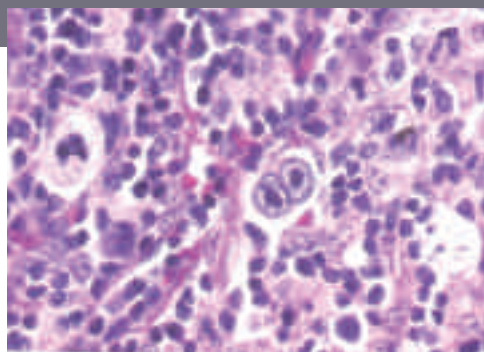
# The Blood and Marrow Transplant Program at Northside Hospital News

SUMMER 2011

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## Brentuximab Vedotin (SGN-35) Demonstrates Significant Activity in Relapsed and Refractory Hodgkin Lymphoma: May Function as a Bridge to an Allograft in Patients Relapsing After High-Dose Chemotherapy



High-dose chemotherapy and autologous stem cell transplantation (HDC-ASCT) is the treatment of choice in patients with Hodgkin lymphoma (HL) who relapse or demonstrate refractory disease following conventional chemotherapy. Overall, 50-60% of such patients are cured following HDC-ASCT. However, this rate is highly dependent on factors evident prior to HDC-ASCT. Patients with initial complete remissions of short duration, positive PET scans following salvage therapy and widespread/bulky disease or B-symptoms following relapse have a high risk of disease recurrence following HDC-ASCT. Median survival of patients who relapse following HDC-ASCT is less than 2.5 years. Some patients who relapse following HDC-ASCT may undergo durable disease remissions following an allogeneic hematopoietic cell transplant (allo-HCT).<sup>1,2</sup> However, adequate de-bulking of the disease prior to the allo-HCT is important as the majority of patients can only tolerate a reduced-intensity or non-myeloablative allo-HCT after failing multiple prior therapies including HDC-ASCT. Finding a regimen that is sufficiently

potent to adequately de-bulk the disease prior to all-HCT has been a challenge as patients have often failed multiple prior chemotherapy regimens and have limited hematopoietic reserve when an allo-HCT is considered.

Brentuximab vedotin (SGN-35) is a targeted cytotoxic agent comprising an anti-CD30 monoclonal antibody conjugated to monomethyl auristatin E (MMAE). Brentuximab vedotin delivers MMAE to CD30 expressing malignant cells. Following binding of the antibody to CD30 on the cell surface, the conjugate is internalized through lysosomal degradation and the MMAE is then released by protease cleavage. Released MMAE then disrupts the microtubule network in cells resulting in cell cycle arrest and apoptosis.

In the phase I trial of this agent in CD30 positive lymphomas tumor regression was seen in 86% of evaluable patients and 50% of patients treated at the highest tolerated dose had an objective response 3. In order to confirm these results, a large phase II trial was conducted to assess the efficacy of single-agent brentuximab vedotin (1.8 mg/m<sup>2</sup> given every 3 weeks up to 16 treatment cycles). The results of this trial were reported at the American Society of Hematology 2010 Annual Meeting held in Orlando in December. Patients were required to have CD30 positive HL that had failed prior HDC-ASCT. More than 100 patients were enrolled – [median age 31 (15-77), median previous

chemotherapy regimens - 3.5 (1-13), refractory to last therapy -42%, prior radiation - 66%]. Median number of three weekly cycles received was 9 (range 1-16).

The overall objective response rate as measured by independent review was 75% with a complete response (CR) rate of 34%. Ninety-four percent achieved some tumor reduction and only 3% had progressive disease. Median duration of response and progression-free survival by independent review were 29 weeks (16-52) and 25.1 weeks respectively. Twenty percent of patients discontinued brentuximab vedotin early because of adverse events. Most frequently encountered adverse events > grade 2 were peripheral neuropathy (9% all grade 3), neutropenia (20%), thrombocytopenia (8%) and anemia (6%). Median time to onset of peripheral neuropathy was 27.3 weeks. The neuropathy resolved or improved in 68% after discontinuation of brentuximab vedotin.

A second phase II trial of brentuximab vedotin monotherapy was also reported at the American Society of Hematology 2010 meeting. This trial addressed efficacy in 58 patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL)<sup>5</sup>. Only 26% of these patients had failed prior HDC-ASCT. Overall objective response by independent review was 86% (53% CR) and was similar in ALK negative and ALK positive patients. Median duration of response was not reached at the time of reporting. Toxicities were similar to those seen in the HL trial.

These trials have demonstrated impressive activity of brentuximab vedotin in relapsed and refractory CD30 positive lymphomas. However, the agent does not appear to be curative in this setting and long term use may be limited by toxicity particularly peripheral neuropathy (seen in 55% of patients in the HL study). This agent may represent an important bridge to curative allo-HCT in patients with HL who have failed prior HDC-ASCT.

Currently at NSH-BMT, two clinical trials of brentuximab vedotin are open for accrual:

**NSH 886 (SGN35-005)** – A randomized phase III study of SGN-35 (brentuximab vedotin) and best supportive care versus placebo and best supportive care in the treatment of patients at high risk of residual Hodgkin lymphoma after autologous transplant (ASCT). – This trial will address the efficacy of prophylactic administration of brentuximab vedotin in patients who have recently undergone HDC-ASCT for classical (not lymphocyte predominant) HL.

Eligible patients will be treated starting within 30–45 days of HDC-ASCT and must be considered high-risk as indicated by at least one of the following criteria:

- History of refractory HL (defined as patients progressing on or failing to achieve a complete remission following frontline standard chemotherapy or a combined modality treatment program)
- Relapsed or progressive HL that occurs <12 months from the end of frontline standard chemotherapy or a combined modality treatment program
- Extranodal involvement at time of pre-ASCT relapse (including extranodal extension of nodal masses into adjacent vital organs)

Outpatients will receive a maximum of 16 treatments given once every 21 days.

**NSH 902 (SGN35-010)**—An open-label, treatment-option protocol of brentuximab vedotin in patients with relapsed or refractory Hodgkin lymphoma or relapsed or refractory systemic anaplastic large cell lymphoma

- The study is open to patients who were on the placebo arm and experienced progression of HL while participating in the NSH 866/SGN35-005 clinical study.
- Additionally, the study is open to patients with relapsed or refractory HL who have previously received an autologous or allogeneic SCT, including patients who did not participate in study SGN35-005, and patients with relapsed or refractory ALCL



- Patients in this study may receive brentuximab vedotin (SGN-35) as long as, in the investigator's judgment, they are continuing to experience a clinical benefit until brentuximab vedotin becomes commercially available.

Outpatients will receive a maximum of 16 treatments given once every 21 days.

For further information regarding these trials, please contact Stacey Brown at [stacey.brown@northside.com](mailto:stacey.brown@northside.com) or (404) 851-8238.

References:

1. Laport GG. Allogeneic hematopoietic cell transplantation for Hodgkin lymphoma: a concise review. *Leuk Lymphoma*. 2008;49:1854-1859.

2. Peggs KS, Kayani I, Edwards N, et al. Donor lymphocyte infusions modulate relapse risk in mixed chimeras and induce durable salvage in relapsed patients after T-cell-depleted allogeneic transplantation for Hodgkin's lymphoma. *J Clin Oncol*. 2011;29:971-978.

3. Younes A, Bartlett NL, Leonard JR, et al. Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas. *N Engl J Med*. 2010;363:1812-1821.

4. Chen R, Gopal AK, SE S. Results of a pivotal phase 2 study of brentuximab vedotin (SGN-35) in patients with relapse or refractory Hodgkin lymphoma. Program and abstracts of the 52nd American Society of Hematology Annual Meeting and Exposition. 2010:Abstract 283.

5. Shustov AR, Advani R, P B. Complete remissions with brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large cell lymphoma. Program and abstracts of the 52nd American Society of Hematology Annual Meeting and Exposition, December 4-7, 2010; Orlando, FL. 2010:Abstract 961.



**Northside Hospital Charity Golf Classic Highlights**  
*Dr. Kent Holland holds first place for the longest drive on the Highlands course at the Atlanta Athletic Club. The 19th annual corporate fundraiser generated more than \$275,000 for the NSH-BMT and Central Research programs.*

## NSH-BMT Program Sponsors Blood & Marrow Transplant BMT InfoNet's Fourth National Survivorship Symposium

The NSH-BMT Program is pleased to be a Gold Level Sponsor of the BMT InfoNet's Fourth National Survivorship Symposium to be held in Atlanta, Ga., on Sept. 10 – 11, 2011 at the Sheraton Atlanta Hotel.

The Blood & Marrow Transplant Information Network (BMT InfoNet) is an organization dedicated to providing stem cell transplant patients, survivors and their loved ones emotional support and access to quality information about stem cell, bone marrow and cord blood transplants.

"We're delighted to partner with the BMT Program at Northside Hospital on this extraordinary two-day seminar," said Sue Stewart, executive

director of BMT InfoNet. "There are so many issues that arise after transplant – medical, emotional, and financial – and survivors often don't know where to turn for help. This symposium will provide survivors with resources to help them better navigate their survivorship experience."

This two-day survivorship symposium recognizes and honors all BMT transplant survivors, caregivers and family members. Dr. Kent Holland, BMT physician for NSH-BMT, and other transplant physician experts in the Southeast, will lead talks about how a transplant survivor can manage the numerous healthcare situations.



*"Thank you so much. This was the BEST experience I've had since my mother got AML six months ago. Words cannot describe how grateful I am to BMT InfoNet."*

**Event Details:**

Register online at:  
[bmtinfolnet.org/atlanta2011](http://bmtinfolnet.org/atlanta2011)  
To register by phone,  
call 1-888-597-7674

**Registration Fee:**

**\$25 for each registrant**  
*Scholarships are available for survivors and one family member (or two parents of a pediatric survivor) who are unable to pay the registration fee.*

**Registration Fee Includes:**

- All conference materials and handouts
- Saturday afternoon snack, dinner and entertainment

“Survivors and their loved ones who attend these symposiums learn so much, both from the medical experts, as well as from each other, on how to live well after transplant,” said Stewart. “It is an extraordinary event for anyone who has been through a bone marrow, stem cell or cord blood transplant.”

Sessions will be repeated throughout each day to ensure that transplant survivors can participate in all sessions. Many of the NSH-BMT program staff members will be participating in these sessions. One of the discussions led by a NSH-BMT staff member is ‘Riding the Emotional Roller Coaster of Survival’ by health psychologist Dawn Speckhart, Ph.D.

In addition, NSH-BMT staff and conference participants will be part of break-out group sessions to discuss various BMT related topics in a more intimate setting. These break-out sessions allow survivors to openly discuss with other survivors their daily triumphs and struggles post-transplant. On the evening of Sept. 10, 2011, there will be a dinner and reception with entertainment.

“Regardless of what type of transplant you had or when you had it, you’ll learn a lot at this symposium,” said Stewart. “We have assembled an incredible team of experts to address the myriad of issues that can arise both in the short and long term after transplant, and sharing your own wisdom and experience with other survivors is a wonderful opportunity as well.”



**NSH-BMT Program and Piedmont Transplant Institute to Sponsor OptumHealth’s Transplant Spotlight Conference**

The NSH-BMT Program will collaborate with Piedmont Hospital’s Transplant Institute for an OptumHealth Spotlight Transplant Conference at the Georgia Aquarium on Oct. 27-28, 2011. The NSH-BMT Program’s physicians and staff will present novel approaches to BMT, updates on new technologies and clinical trials in BMT.

The conference attendees will include physicians, case managers and allied health care professionals. An early evening cocktail reception will be

held on Thursday, where attendees can meet staff and take a self-guided tour of the Georgia Aquarium.

In 2009, OptumHealth, a large national health insurance provider, began to partner with its Centers of Excellence transplant programs to sponsor educational symposiums. These symposiums are organized to showcase a transplant center’s contributions in advancing the field of BMT; to review state-of-the-art clinical research

trials; and to provide attendees with opportunities to obtain continuing education credits.

“OptumHealth’s Spotlight Conferences are an integral part of the relationships we build and maintain with medical centers,” said Rob Webb, chief executive officer of OptumHealthcare Solutions. “We are particularly excited to be able to bring Northside Hospital and Piedmont Hospital together for the purpose of educating clinicians on cutting edge topics surrounding solid organ

and blood/marrow transplantation - and the importance of timely and appropriate referral.”

The NSH-BMT Program and Piedmont Transplant Institute are the only transplant programs in the Southeast to sponsor an OptumHealth Spotlight conference. “This is an important event from a clinical and medical management standpoint,” said Webb.

Event will be held at the Georgia Aquarium on Oct. 27-28, 2011 from 8:00 a.m. until 4:00 p.m. View event details at [www.myoptum-healthcomplexmedical.com](http://www.myoptum-healthcomplexmedical.com)

## Role of NSH-BMT Program’s Clinical Pharmacy Specialists (PharmDs) - Improving Patient Outcomes

The NSH-BMT Program employs five dedicated full time PharmDs. This is an unusually extensive level of support compared to other, similarly sized BMT programs, and is part of the program’s dedication to quality outcomes. These PharmDs provide comprehensive inpatient and outpatient pharmaceutical services, helping prevent medication errors, improve quality care initiatives, and help conduct clinical research. The level of PharmD support available to the program is an important contributing factor in generating the superior patient survival outcomes that NSH-BMT is known for as published by the National Marrow Donor Program ([www.marrow.org](http://www.marrow.org)).

### Patient Education

Each patient receives extensive pharmacy education prior to starting chemotherapy. The BMT PharmDs discuss individual medications and provide recommendations to patients during outpatient clinic visits and their inpatient stay. Patients discharged from inpatient care receive a detailed medication list to establish a smooth transition to outpatient therapy.

### Clinical Services

During inpatient and outpatient rounds, PharmDs work closely with the BMT physicians to ensure safe and effective medication use by monitoring drug therapy, interactions, adverse effects, and

dose adjustments; and bridge inpatient and outpatient environments with a detailed patient history report.

Maintaining more than 20 supportive care treatment algorithms provides another component to improving patient outcomes. These algorithms, which are researched from a clinical and pharmacoeconomic perspective, are presented at a multidisciplinary meeting before receiving final approval by the BMT physicians. Strict adherence to these algorithms is critical in the achievement of cost effective and quality patient care, resulting in superior patient survival outcomes.

### Medication Deviation Prevention

Active roles in medication variance prevention:

- Development of preprinted chemotherapy orders, supportive care treatment algorithms, and standard operative procedures.
- Oversight of outpatient IV preparations.
- Serving on an interdisciplinary team that includes a BMT physician, two BMT PharmDs and a nurse to review and validates preprinted chemotherapy orders.
- Oversees outpatient pharmacy operations, developing standard operating procedures to prevent dispensing errors and to maintain an aseptic product.
- Checking all chemotherapy products prior to administration.



*Connie Sizemore, Lead BMT PharmD; Ron Mihelic, PharmD; Melissa Sanacore, Lead BMT/Leukemia Research PharmD; Justin LaPorte, PharmD; Mindy Leech, PharmD.*

## Investigational Drug Pharmacy and Research

The roles of a BMT PharmD clinical research pharmacist include:

- Developing investigational drug orders to assure compliance with study protocols, minimizing the risk of chemotherapy administration errors associated with study medications.
- Continuous communication with the BMTGA MD investigator prior to the initiation of a clinical trial and throughout the conduct of the trial, ensuring adherence with clinical research investigational study protocols.
- Developing institutional research protocols unique to the NSH-BMT Program.



## Academic Activities

Several of the BMT PharmDs hold adjunct faculty positions at Mercer University and the University of Georgia. Professional development and training of pharmacy residents, pharmacy students, and nursing staff are essential components of the BMT clinical pharmacy program. The PharmDs of the BMT program are also active in presenting research at annual meetings including the American Society of Hematology and the annual Tandem BMT meeting as well as in authoring research publications from the program.

## Recent Abstracts Presented by NSH-BMT PharmDs:

Sizemore CA, LaPorte J, Holland HK, Mccollum, J, Westerman, Morris LE et al. A Comparison of Toxicity and Mobilization Efficacy Following Two Different Doses of Cyclophosphamide for Mobilization of Hematopoietic Stem Cells in

Non-Hodgkin's Lymphoma Patients. *Biology of Blood and Marrow Transplantation* 2010; 16(S2): Abstract 130.

Sizemore CA, LaPorte J, Sanacore MF, Holland HK, Mccollum, J, Westerman et al. A Comparison of Toxicity and Mobilization Efficacy Following Two Different Doses of Cyclophosphamide for Mobilization of Hematopoietic Stem Cells in Multiple Myeloma Patients. *Biology of Blood and Marrow Transplantation* 2010; 16(S2): Abstract 97.

Sizemore CA, Manion K, Morris L, Bashey A, Holland HK, Solomon SR. Total Outpatient Care for Myeloablative Unrelated Donor Hematopoietic Cell Transplantation: A Safe and Effective Alternative to Standard In-Patient Care. *Blood* 2010; 116: Abstract 3525.

Sanacore M, Brown S, Roth C, Zhang M, Smith P, Holland HK et al. 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. *Blood* 2009; 114: Abstract 3371.

Sanacore M, Manion K, Smith P, Xhang Xu, Holland HK, Morris L et al. Improved Survival using Dual Monoclonal Antibody Therapy with Aggressive Anti-Microbial Prophylaxis In Steroid-Refractory Acute Graft-Versus-Host Disease. *Blood* 2010; 116: Abstract 1262.

We believe the NSH-BMT Program's five BMT PharmDs provide essential pharmacy expertise to the clinical transplant program and quality management programs. Ultimately, their efforts have contributed to the program's outstanding survival outcomes.

## Open Clinical Trial Studies

*Clinical trials can also be accessed online at [www.northside.com](http://www.northside.com) or [www.bmtga.com](http://www.bmtga.com).*

*For additional information regarding these trials, please contact Stacey Brown at [stacey.brown@northside.com](mailto:stacey.brown@northside.com) or (404) 851-8238.*

|         |   |
|---------|---|
| NSH 721 | NMDP Recipient Consent for Participation in Registry, Research Database, and Research Sample Repository   |
| NSH 877 | A Phase II Multicenter Trial of Myeloablative Double Unit Umbilical Cord Blood Transplantation (UCBT) in Adults with Hematologic Malignancy   |
| 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 887 | A Multicenter, Randomized, Double Blind, Phase III Trial Evaluating Corticosteroids with MMF vs. Corticosteroids with Placebo as Initial Systemic Treatment of Acute GVHD   |
| NSH 888 | The Impact of Hematopoietic Stem Cell Transplantation on Primary Caregiver Level of Burden and Distress   |
| NSH 890 | Evaluation of Lenalidomide as Maintenance Therapy after Allogeneic Hematopoietic Stem Cell Transplantation for High-Risk Multiple Myeloma   |
| 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 vs. Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma; BMT CTN 0702   |
| NSH 898 | A Randomised Phase III Study of Elacytarabine vs. Investigator's Choice in Patients with Late Stage Acute Myeloid Leukaemia   |
| NSH 902 | An open-label, treatment-option protocol of brentuximab vedotin in patients with relapsed or refractory Hodgkin Lymphoma or relapsed or refractory systemic anaplastic large cell lymphoma  |
| 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 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  |

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### 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. 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

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.

*Referrals can be made by a physician or physician staff member by calling (404) 255-1930. The referring physician will have the option of speaking directly to one of the physicians or a transplant/leukemia coordinator to make the referral. The coordinators will contact the referring physician's 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**  
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# PDF- Acceptance

