PROTOCOL SYNOPSIS - BMT CTN PROTOCOL #0401

Phase III Rituxan/BEAM vs. Bexxar/BEAM with Autologous Hematopoietic Stem Cell Transplantation (ASCT) for Persistent or Relapsed Chemotherapy Sensitive Diffuse Large B-Cell Non-Hodgkin's Lymphoma

Study Chairperson:	Julie M. Vose, M.D.
Primary Objective:	The primary objective of this study is to compare progression-free survival (PFS) after autologous hematopoietic stem cell transplantation (ASCT) for chemotherapy-sensitive diffuse large B-cell lymphoma using Rituxan/BEAM versus Bexxar/BEAM for pre-transplant conditioning.
Secondary Objectives:	Secondary objectives for the comparison are overall survival, time to progression, complete response (CR) and partial response (PR) proportion at Day 100, time to hematopoietic recovery, hematologic function, incidence of infection, maximum mucositis score by Day 21, immune reconstitution, treatment-related mortality, and development of myelodysplasia, secondary acute myelogenous leukemia, or abnormal cytogenetics.
Study Design:	This study is designed as a Phase III, multi-center trial, comparing PFS after autologous hematopoietic stem cell transplantation using a standard Rituxan plus BEAM transplant regimen versus a regimen adding Bexxar to BEAM.
Accrual Objective:	The trial will accrue 224 patients randomized equally between two treatment arms.
Accrual Period:	The estimated accrual period is two years.
Eligibility Criteria:	Eligible patients are 18-80 years of age with Karnofsky performance status $\geq$ 70% that have persistent or recurrent diffuse large B-cell lymphoma. Patients must have received 1-3 prior treatment regimens, including an induction chemotherapy and $\leq$ 2 salvage regimens. Monoclonal antibody therapy and local radiation will not be counted as prior therapies. Patients must have chemosensitive disease as demonstrated by at least a partial response (as defined by the criteria in Chapter 3) to induction or salvage chemotherapy. Patients must also have $\leq$ 20% BM involvement after their most recent salvage therapy. Patients cannot have transformed follicular lymphoma, evidence of MDS/AML, had prior autologous or allogeneic HSCT, or received prior radioimmunotherapy. Patients must also initiate conditioning therapy within 3 months of mobilization. Mobilization therapy may be employed per institutional guidelines, but all patients must receive one dose of Rituxan (375 mg/m^2) within 3 months prior to actual stem cell apheresis. Patients must have an adequate autograft (target $\geq$ 2.0 X

	10^6 CD34+ cells/kg; minimum $\geq$ 1.5 X 10^6 CD34+ cells/kg) to be eligible for the protocol.
Treatment Description:	Eligible patients will be randomized to receive either: 1.) Rituxan plus BEAM, with Rituxan 375 mg/m^2 IV Days -19 and -12, BCNU 300 mg/m^2 Day -6, Etoposide 100 mg/m^2 BID Days -5 to -2, Cytarabine 100 mg/m^2 BID Days -5 to -2, and Melphalan 140 mg/m^2 Day -1 followed by ASCT; or, 2.) Bexxar/BEAM with the dosimetric dose of 5 mCi Bexxar on Day -19 and the therapeutic dose calculated to administer 75 cGy total body dose (TBD) on Day -12. Patients will then receive BCNU 300 mg/m^2 Day -6, Etoposide 100 mg/m^2 BID Days -5 to -2, Cytarabine 100 mg/m^2 BID Days -5 to -2, and Melphalan 140 mg/m^2 Day -1 followed by ASCT.
Study Duration:	Patients will be followed for at least two years post-ASCT.

TREATMENT SCHEMA