

**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 30, 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 = 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 response to induction or salvage chemotherapy by achieving a = 50% reduction in estimated lymph node volume and a reduction in lymph node axial diameter to  $\leq 3$  cm OR = 75% reduction in estimated lymph node volume. Patients must also have = 20% BM involvement after their most recent salvage therapy.
- Treatment Description:** Within 6 weeks of enrollment, all patients will receive cyclophosphamide  $4 \text{ gm/m}^2$  on Day 2 concomitantly with Rituxan  $375 \text{ mg/m}^2$  on Days 1 and 8. G-CSF  $10 \text{ } \mu\text{g/kg/day}$  subcutaneously will be given starting 2 days after the initiation of cyclophosphamide and continue until leukapheresis is complete. Patients will undergo leukapheresis upon blood count recovery. Patients must have an adequate autograft (target =  $2.0 \times 10^6$  CD34+ cells/kg; minimum

$\geq 1.5 \times 10^6$  CD34+ cells/kg) to proceed further on the protocol. After obtaining an adequate graft, patients will be randomized to receive either: 1.) Rituxan plus BEAM, with Rituxan 375 mg/m<sup>2</sup> IV Days -19 and -12, BCNU 300 mg/m<sup>2</sup> Day -6, Etoposide 100 mg/m<sup>2</sup> BID Days -5 to -2, Cytarabine 100 mg/m<sup>2</sup> BID Days -5 to -2, and Melphalan 140 mg/m<sup>2</sup> 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<sup>2</sup> Day -6, Etoposide 100 mg/m<sup>2</sup> BID Days -5 to -2, Cytarabine 100 mg/m<sup>2</sup> BID Days -5 to -2, and Melphalan 140 mg/m<sup>2</sup> Day -1 followed by ASCT.

**Study Duration:**

Patients will be followed for at least two years post-ASCT.

## TREATMENT SCHEMA

