PROTOCOL SYNOPSIS - BMT CTN PROTOCOL #0202

Autologous vs. Non-Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Patients with Chemosensitive Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response or First Partial Response

Study Co-Chairpersons:	Ginna Laport, M.D. and Robert Negrin, M.D.
Accrual Objective:	A minimum of 80 patients with recurrent follicular non-Hodgkin's lymphoma (REAL classification follicle center lymphoma, follicular grades I and II or patients with histologically confirmed WHO classification follicular lymphoma grades 1, 2, 3a or 3b) and an HLA-matched sibling will be entered on the protocol. It is expected during the same period that an additional 187-320 patients without an HLA-matched sibling will be entered on the protocol.
Study Design:	This study is designed as a Phase II/III, multi-center trial, comparing two transplant strategies to determine whether non-myeloablative allogeneic HSCT will improve long-term progression-free survival compared to autologous HSCT. Recipients will be biologically assigned to the appropriate treatment arm depending on the availability of an HLA-matched sibling.
Accrual Period:	The estimated accrual period is three years.
Primary Objective:	The primary objective is to compare progression-free survival (PFS) at three years between the two treatment arms.
Secondary Objectives:	Secondary objectives for the comparison of non-myeloablative allogeneic HSCT vs. autologous HSCT are three-year overall survival, time to progression, time to complete response (CR) and partial response (PR), time to off-study therapy, incidence of infections, and incidence of NCI Common Terminology Criteria Adverse Events (CTCAE) Version 3.0 Grade ≥ 3 toxicities. Secondary objectives for the non-myeloablative allogeneic HSCT recipients include incidence and severity of acute and chronic GVHD, and incidence of primary and secondary graft failure. The efficacy of cyclophosphamide plus rituximab *in vivo* purging will also be evaluated as well as the prediction of disease relapse by measurement of t(14;18) by quantitative polymerase chain reaction (PCR). Quality of life as measured by the SF-36 and the FACT-BMT will be described in both patient populations.
Eligibility Criteria:	Eligible patients are ≤ 75 years of age with Karnofsky performance score $\geq 70\%$ who have histologically confirmed recurrent follicular lymphoma (REAL classification follicle center follicular grades I and II or patients with histologically confirmed WHO classification follicular lymphoma grades 1, 2, 3a or 3b). Patients must have received ≤ 3 prior treatment regimens. Monoclonal antibody therapy

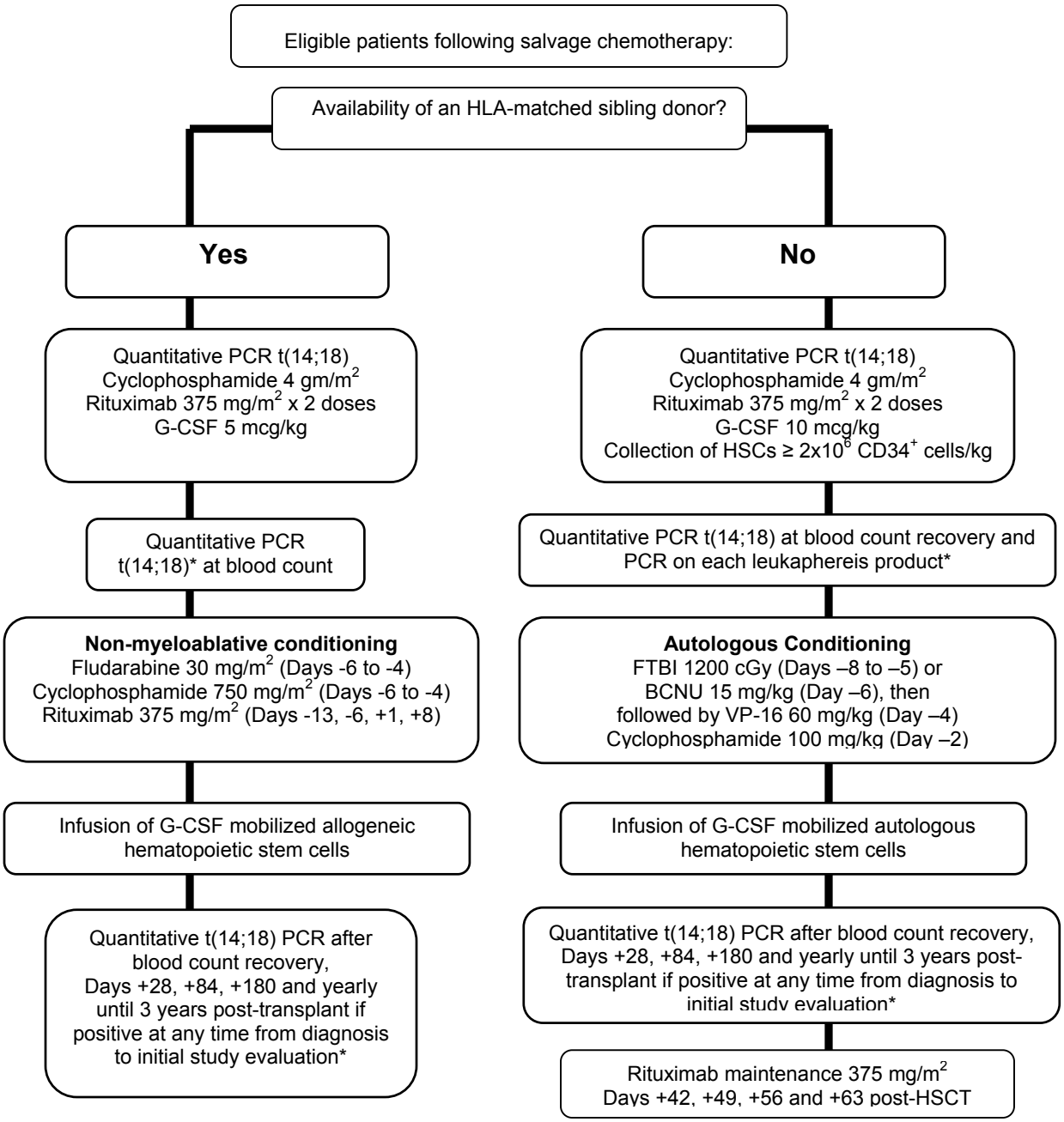
and local radiation will not be counted as prior therapies. Patients must demonstrate chemosensitive disease by achieving reduction in lymph node axial diameter to < 3 cm or > 50% reduction in estimated lymph node volume AND ≤ 20% BM involvement after their most recent salvage therapy. Patients do not have to express t(14;18).

Treatment Description: Within 4 weeks of enrollment and after HLA typing and evaluation of potential sibling donors is complete, all patients will receive cyclophosphamide 4 gm/m^2 on Day 2 concomitantly with rituximab 375 mg/m^2 on Days 1 and 8. G-CSF 10 mcg/kg/day (autologous patients) or 5 mcg/kg/day (allogeneic patients) SQ or IV will be given starting 2 days after the initiation of cyclophosphamide. Patients assigned to the autologous HSCT arm will undergo leukapheresis upon blood count recovery. After the mobilization process is complete, autologous patients will then receive either fractionated total body irradiation (FTBI) 1200 cGy or BCNU 15 mg/kg. VP-16 60 mg/kg and cyclophosphamide 100 mg/kg will also be given followed by autologous HSCT. Patients must have an adequate autograft defined as ≥ 2.0 x 10^6 $CD34^+$ cells/kg. Rituximab 375 mg/m^2 x 4 weekly doses, to begin on approximately Day +42, will be given as maintenance therapy. Patients with an HLA-matched sibling will receive a non-myeloablative conditioning regimen of fludarabine 30 mg/m^2/day and cyclophosphamide 750 mg/m^2/day from Day -6 to -4 followed by infusion of G-CSF mobilized donor hematopoietic stem cells. Rituximab 375 mg/m^2 will be administered on Day -13, -6, +1 and +8. GVHD prophylaxis will consist of tacrolimus (IV or PO) until Day +90 followed by a taper and methotrexate 5 mg/m^2 IV on Day +1, +3, and +6 post-HSCT. All patients will undergo PCR analysis for t(14:18) from the peripheral blood after blood count recovery from the cyclophosphamide/rituximab cytoreductive/mobilization regimen and on Day +28, +84, +180 and yearly post-HSCT if positive at any time from diagnosis to initial study evaluation.

Quality of Life: The FACT-BMT and MOS SF-36 instruments will be used to describe the health-related quality of life (HQL) of patients. A secondary analysis will compare the HQL between the two treatment arms. The self-report questionnaire will be performed prior to cytoreductive/ mobilization therapy and at two years post-HSCT for English and Spanish speaking patients only.

Study Duration: Patients will be followed for at least three years post-HSCT.

TREATMENT SCHEMA



* Only required for patients who had a positive PCR at any point prior to study entry or at the baseline screen on study.