PROTOCOL SYNOPSIS – BMT CTN PROTOCOL 0102

A Trial of Tandem Autologous Stem Cell Transplants +/- Post Second Autologous Transplant Maintenance Therapy Versus Single Autologous Stem Cell Transplant Followed by Matched Sibling Non-myeloablative Allogeneic Stem Cell Transplant for Patients with Multiple Myeloma

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Study Design:	The study is designed as a Phase III, multi-center trial of tandem autologous transplants versus the strategy of autologous followed by HLA-matched sibling non-myeloablative allogeneic transplant. Study subjects will be biologically assigned to the appropriate arm depending on the availability of an HLA-matched sibling. There is a nested randomized phase III trial of observation versus maintenance therapy following the second autologous transplant for patients on the tandem autologous transplant arm.
Primary Objective:	Post-tandem autologous transplant randomized trial of maintenance versus observation: The primary objective is to compare progression-free survival at three years between the two arms. Tandem autologous transplants versus autologous transplant followed by HLA-matched sibling non-myeloablative allogeneic transplant: The primary objective is to compare progression-free survival at three years between the two arms.
Secondary Objectives:	Post-tandem autologous transplant randomized trial of maintenance versus observation: Secondary objectives are to compare 'current' myeloma-stable survival, three-year overall survival, and incidence of progression. Tandem autologous transplants versus autologous transplant followed by HLA-matched sibling non-myeloablative allogeneic transplant: Secondary objectives are to compare 'current' myeloma-stable survival, three year overall survival, and incidence of progression.
Tertiary Objectives:	Post-tandem autologous transplant randomized trial of maintenance versus observation: Tertiary objectives include complete remission (CR) rate and CR+partial remission (PR) rate at 2 and 12 months after the second transplant, time to CR and CR+PR, time to off-study therapy, rate of discontinuation of maintenance therapy and duration of maintenance therapy, incidence of toxicities Grade ≥ 3 according to the CTCAE Version 3.0, incidence of infections and quality of life. Tandem autologous transplants versus autologous transplant followed by HLA-matched sibling non-myeloablative allogeneic transplant: Tertiary objectives include CR and CR+PR rates at 2 and 12 months after the allograft, time to CR and CR+PR, time to second transplant, time to off-study therapy, and quality of life. Other tertiary outcomes to be evaluated only in the allogeneic transplant arm will include incidence of both primary and secondary graft failure and incidence and severity of graft-versus-host-disease.

Eligibility Criteria: Eligible patients are ≤ 70 years of age with Karnofsky scores ≥ 70, who meet Durie and Salmon criteria for diagnosis of multiple myeloma, who have symptomatic MM requiring treatment, who have received at least three cycles of systemic therapy and who are within 2-10 months of initiation of the initial therapy (this time frame excludes the time for mobilization therapy). Patients must have available an autograft ≥ 4.0 x 10^6 CD34+ cells/kg patient weight unless it is known prior to enrollment that they will receive an allogeneic transplant after their initial autologous transplant. Patients with a consenting, eligible HLA-matched sibling must have an autograft ≥ 2.0 x 10^6 CD34+ cells/kg patient weight.

Treatment Description: Mobilization therapy will not be specified for the study. All patients will undergo a first autologous peripheral blood stem cell (PBSC) transplant with high-dose melphalan (200 mg/m^2 IV/day) given on Day –2. Melphalan will be given between 2 and 8 weeks after initiation of mobilization therapy.

Patients with adequate recovery will receive either a second autologous PBSC transplant or a non-myeloablative PBSC allogeneic transplant from an HLA-matched sibling. This post-transplant therapy will be initiated at least 60 days (preferably 60-120 days) following the initial autologous transplant.

Patients without an HLA-matched sibling donor will be randomized to either observation or one year of maintenance therapy with dexamethasone and thalidomide to begin following recovery from their second autologous PBSC transplant. This post-transplant therapy will be initiated at least 60 days (preferably 60-120 days) following the second autologous transplant.

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 questionnaires will be performed prior to both transplants and post second transplant at six months and yearly until three years for English and Spanish speaking patients only.

Accrual Objective: Study accrual and analysis is based on the number of standard risk multiple myeloma patients with an available HLA-matched sibling donor. A total of 150 standard risk multiple myeloma patients with an HLA-matched sibling donor will be accrued. During this time, it is expected that at least 350 standard risk multiple myeloma patients without a sibling donor will also be entered on the trial. In addition, high-risk patients with and without HLA-matched siblings will also be entered on the trial during the same period.

Accrual Period: The estimated accrual period is three years.

Study Duration: Patients will be followed for at least three years after their second transplant.

Outline of Treatment Plan