PROTOCOL SYNOPSIS – BMT CTN PROTOCOL 0902

A Phase III Randomized, Multicenter Trial Testing Whether Exercise or Stress Management Improves Functional Status and Symptoms of Autologous and Allogeneic Recipients

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Study Design: Phase III, randomized, unblinded, multicenter, prospective comparative study of exercise, stress management, the combination of exercise and stress management versus standard care to improve functional status and symptoms.

Patients complete baseline measures and are randomized to one of the four arms, stratified by center and type of transplant procedure (autologous/syngeneic, myeloablative allogeneic, reduced intensity/non-ablative allogeneic). The exercise and stress management interventions are designed to be self-administered after a brief, 10-15 minute training session.

Endpoint assessment will occur at 100 days +/- 14 days and 6 months +/- one month

Primary Objective: To determine whether exercise or stress management improves self-reported physical and mental functioning compared to standard care at 100 days using an intention to treat analysis

Secondary Objectives:

a) To determine whether exercise or stress management improves physical and mental functioning compared to standard care at 100 days, limiting the analysis to patients who survive and provide a Day 100 self-assessment (conditional analysis with main effects)

b) To compare physical and mental functioning among the 4 groups using pair-wise comparisons, limiting the analysis population to patients who provide a Day 100 self-assessment (pair-wise conditional analysis)

c) To compare symptoms (fatigue, pain, sleep, nausea, cancer and treatment distress) at 100 days among patients who provide a Day 100 self-assessment (conditional analysis)

d) To compare the number of hospital days within the first 100 days

e) To assess durability of effects by comparing functional status and symptoms at 6 months

f) To compare overall survival at 6 months

Eligibility:

Inclusions:

a) Age 18 years or older.

b) Able to speak and read English.

c) Able to exercise at low to moderate intensity - adequate cardiopulmonary reserve, as judged by self-reported ability to walk up one flight of stairs, no requirement for supplemental oxygen, and physician judgment.

d) Willing and able to provide informed consent.

e) Stated willingness to comply with study procedures and reporting requirements.

f) Planned autologous or allogeneic transplantation within 6 weeks.

Exclusions:

a) Orthopedic, neurologic or other problems which prevent safe ambulation and protocol adherence.

b) Participation in another clinical trial with quality of life or functional status as a primary endpoint.

c) Planned anti-cytotoxic therapies, other than TKI, Gleevac or Rituximab OR unless pre-approved by the protocol chair, within 100 days post-transplant.

d) Planned DLI within 100 days post-transplant.

e) Planned tandem transplant (autologous/autologous or autologous/allogeneic).

Treatment Description: **Exercise.** The goal is to have participants exercise by walking 3 to 5 times per week for at least 20 to 30 minutes at a maximum intensity of 50 to 75% of their estimated heart rate reserve.

Stress management. The goal is to have participants practice paced abdominal breathing, progressive muscle relaxation with guided imagery, and use of coping self-statements to decrease stress.

Standard care will follow institutional guidelines that reflect standard practices

All 4 groups will receive a general informational DVD about hematopoietic cell transplantation.

Accrual Objective: 700 subjects will be randomized approximately 1:1:1:1 across the four study arms.

Accrual Period: The estimated accrual period is 36 months.

Study Duration: Patients will be followed for 6 months after transplantation.

Statistical issues: The primary objectives of the study are to compare physical functioning and mental functioning between the groups who do or do not receive exercise training and between the groups who do or do not receive stress management training (factorial design). The sample size calculation is based upon having 85% power to detect differences of 0.5 STD in the primary endpoint between groups (exercise vs. no exercise or stress management vs. no stress management) after splitting the type I error rate across these 4 primary comparisons. This analysis controls for baseline assessment and clinical characteristics and accounts for cancelled transplants and missing data using an Intention-to-Treat analysis. Randomization will be stratified for balance based on center and type of transplant (autologous, myeloablative allogeneic, and non-myeloablative allogeneic groups).