BMT CTN 0102 Version 7.0 (5/15/2006)

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

Changes to Patient Consent

- The number of patients to be enrolled has been updated to 800.
- A statement was added to the Treatment Arm B section, regarding maintenance therapy, "Results from two recent studies show that thalidomide may slow the rate of relapse after autologous transplantation. These studies show that time to worsening disease may be longer in patients who get thalidomide. In these studies, thalidomide did not prolong survival, and did increase the number of side effects. The dose and timing of thalidomide was different in these reported studies than in this study. We do not know if it is better to wait until a relapse occurs to use this drug. We also do not know whether thalidomide will significantly affect quality of life."
- A list of alternative therapies was updated in *§13 What other options or treatments are available if you do not want to be in this study:*
  "Current therapies for multiple myeloma include:
  - Chemotherapy using single drugs or combinations of drugs;
  - Single autologous transplants with or without additional drugs to prevent relapse after transplantation;
  - Double autologous transplants with or without additional drugs to prevent relapse after transplantation;
  - Allogeneic transplantation using a related or unrelated donor

  You may also be eligible to receive other investigational treatment or you may decide not to receive any treatment. Your doctor will discuss these other possible treatment approaches with you."

Significant Changes to Version 5.0 of the Protocol

- In *§2.3.1 Initial Patient Eligibility Criteria*, added "or O_2 saturation >92% of room air" to the pulmonary inclusion criterion.
- In *§2.3.2 Initial Patient Exclusion Criteria,* updated the exclusion criterion "Karnofsky performance score less than 70% unless approved by the Medical Monitor or one of the Protocol Chairs."
- In *§2.3.2 Initial Patient Exclusion Criteria,* added an exclusion criterion "Prior organ transplant requiring immunosuppressive therapy."
- MMF dosing was changed to be based on ideal body weight (IBW) for patients who weigh 100-120% of their IBW, based on actual body weight (ABW) for patients who weigh less than 100% of their IBW, and based on adjusted ideal body weight (AIBW) for patients who weigh more than 120% of their IBW. This is reflected in *§2.4.4.2 Peri-nonmyeloablative allogeneic transplant immunosuppression.*

- The definitions of engraftment, primary graft failure, and secondary graft failure have been update in *§3.10.1 Incidence of Primary and Secondary Failure*, as indicated in strike-out text:
    - Engraftment is defined as achieving > ~~10~~ 5% donor ~~peripheral blood T cell~~ chimerism by Day 56.
    - Primary graft failure is defined as donor ~~peripheral blood T cell~~ chimerism <5% by Day 56 post-transplant.
    - Secondary graft failure is defined by documented engraftment followed by loss of graft as defined by donor ~~peripheral blood T cell~~ chimerism <5% as demonstrated by a chimerism assay.
- In *§4.2.4.1 Evaluations prior to the first autologous transplantation* and *§4.2.4.3 Evaluations prior to the second autologous transplant* added that 0_2 saturation may be reported instead of DLCO, FEV1, and FVC.
- In *§4.2.4.1 Evaluations prior to the first autologous transplantation, §4.2.4.4 Post second transplant evaluations* and *Appendix C Laboratory Procedures* clarified that cytogenetic studies are to be done by standard metaphase karyotype analysis.
- A plan to pool the centers with fewer than two standard risk patients on the allograft arm at the close of enrollment was added to *§5.2.3 Effects of Clinical Center.*
- A paragraph describing monitoring of key safety endpoints and notification of the Data and Safety Monitoring Board if rates exceed pre-set thresholds was added to *§5.4 Statistical Stopping Guidelines.*
- The definition of engraftment was updated in *§5.5.4 Analyses Within Each Treatment Arm.*

Administrative Changes to Version 5.0 of the Protocol

- Marcelo Pasquini, M.D. has been added to the protocol team. This is reflected in the title page.
- New centers have been added to the list of participating centers.
- Several typographical errors were corrected in *Appendix A – Durie and Salmon Criteria for the Initial Diagnosis and Staging of Multiple Myeloma*.
- Contact information for the NHLBI repository has been updated in *Appendix C – Laboratory Samples.*