SCREENING CONSENT

BMT CTN 0702
A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma

Study Sponsor: This study is sponsored the National Institutes of Health (NIH): the National Heart, Lung, and Blood Institute (NHLBI) and National Cancer Institute (NCI) by providing financial support for this study through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).

Principal Investigator: (site specific PI)

24-Hour Phone: <Insert 24-hour contact information>

This is a clinical trial, which is a research study to answer specific medical questions. Your doctor (the person in charge of the research) will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with family and friends. You can also discuss this with your health care team. If you have any question, you can ask the study doctor for more information.

INTRODUCTION

This is a screening informed consent for a clinical trial in multiple myeloma. This trial includes the option to patients to provide samples for important research on multiple myeloma and transplant. At this stage we are asking you consent to provide a bone marrow sample for research. This is not the informed consent for the clinical trial.

Some transplant centers perform routine bone marrow biopsy and aspirate prior to decide to offer patients clinical trials. In order to avoid repeating the bone marrow examination after patients are registered to participate in the clinical trial, we are asking consent for collection of an additional volume of bone marrow for research related to this clinical trial. In case you are not eligible for the clinical trial or decide against participating, this sample of your bone marrow will be discarded.

If you sign this screening consent, your bone marrow sample will be utilized by the BMT CTN for future research.

CLINICAL TRIAL SUMMARY

This screening process is for the research protocol entitled: "A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma" or STaMINA (Stem Cell Transplant in Myeloma Incorporating Novel Agents) trial. You are being asked to take part in this research study because you have multiple myeloma (MM), a cancer of the bone marrow. The study is designed to test different treatments for patients with multiple myeloma.

A separate consent form will be provided to you describing the full research study in detail. You will have the opportunity to have all of your questions answered prior to deciding to participate.

By agreeing to take part in the screening tests, the investigators cannot promise that you will be able to take part in the research study. Also, by agreeing to take part in the screening, you will allow your physician to collect an additional volume of bone marrow aspirate for research. No additional bone marrow aspirates prior to your transplant will be required. The sample for research will be collected in addition to the amount collected by your doctor for routine tests to assess if there are cancer cells in your bone marrow. You can still decide not to participate in the research study, in which case this additional volume of bone marrow will be discarded.

If after completion of the screening, you are found to be eligible for participation in the research protocol, you will be asked to consider participation in the full treatment research protocol. Prior to you agreeing to participate and signing the consent form for the treatment research protocol, you will have the opportunity to discuss the study with your transplant physician. Signing either this screening consent form or the treatment research consent form does not in any way obligate you to participate in this research protocol. Participation in this screening process does not guarantee inclusion in the treatment research protocol.

YOUR PARTICIPATION IS VOLUNTARY

Once you understand the screening process and agree to take part, you will be asked to sign this consent form. You will be given a copy of this consent form to take with you for your records. It is important that you understand that ***your participation is completely voluntary,*** and that ***you may decide to drop out of the study at any time*** without losing the benefits of your regular medical care.

RISKS AND/OR DISCOMFORTS

Below is a summary of known risks with the invasive screening procedures. The risks and discomforts of the procedures will be explained by the doctor who does the procedures and another consent form must be signed for any invasive tests. Listed below are specific invasive procedures that are done at screening and may be repeated later if necessary.

Bone Marrow Aspiration and Biopsy: A bone marrow aspiration is a procedure in which an area of the hip (buttock area) is numbed with local anesthetic, and a small sample of bone marrow is withdrawn. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle. When the local anesthesia is given, you may initially feel a

burning sensation in your skin and bone surface for several seconds. During the actual procedure itself, you may temporarily feel pressure and/or pain of varying degrees. If necessary, you may ask your physician for additional local anesthesia or a medication to ease your stress. You also may experience bleeding, and/or bruising after the procedure is completed and you may experience soreness in the area for a few days afterwards. Rarely an infection can develop.

POTENTIAL BENEFITS
Although this study cannot be guaranteed to be of benefit to you, it is hoped that your taking part may lead to the improvement or "temporary" disappearance of your myeloma and prolongation of your life. However, no benefit is guaranteed.

COSTS TO THE SUBJECT (YOU)
There are no additional costs to you to provide bone marrow sample for future research.

RESEARCH-RELATED INJURY
If you should be injured as a result of your participation in this study, emergency medical care is available to you at the usual charge. The hospitals and/or treating physicians reserve the right to bill you and/or your insurance provider(s) for services you receive for the injury. There is no provision for free medical care or monetary compensation from the study sponsor, The National Institutes of Health.

PAYMENTS (REIMBURSEMENT)
You will not be paid for taking part in this study. You will be reimbursed for travel expenses related to study-related evaluations and/or treatments only as explained above under the COSTS TO THE SUBJECT (YOU) section.

CONFIDENTIALITY
We will try to keep your personal information as private as we can. There is no guarantee of absolute privacy. Your personal information may be disclosed if required by law. We will keep track of your medical information after you return home. Organizations that are listed below may inspect or copy your research records for quality assurance and data analysis. Your research records will identify you by name and will include things such as your medical history, results of your blood tests and exams, reports from your surgery and treatment, and reports of your office visits.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

SCREENING DESCRIPTION/PROCEDURES

Researchers are trying to learn more about multiple myeloma and other health problems. Much of this research is done using human tissue or blood. These samples are collected during the clinical trial and stored for future use.

You are being asked to let us store some of your bone marrow for possible use in future research and/or for the PRIMeR ancillary study (Prognostic Immunophenotyping in Myeloma Response). The samples collected for future research and the samples collected for the PRIMeR ancillary study can be done at the same time.

Future Research Samples

Your bone marrow samples for future research will be collected at your transplant center during the period you are participating in this study and kept at a central place, called the BMT CTN Research Sample Repository (this will be called the "Repository" in the rest of the consent form). A Repository is a place that protects, stores and sends out samples for approved research studies.

Future research bone marrow samples will be collected prior to first autologous transplant and yearly thereafter (4 more times). The bone marrow samples will be collected as part of the scheduled evaluations in the STaMINA clinical trial and routine assessment of your disease.

PRIMeR Ancillary Study Samples

The PRIMeR ancillary study will be conducted along with the STaMINA clinical trial. All patients who participated in the STaMINA clinical trial are eligible to participate in the PRIMeR ancillary study. This study will use a technique called flow cytometry to look for small quantities of myeloma cancer cells in your bone marrow. This method has been shown in previous studies to help doctors predict which patients will have a longer period without their myeloma coming back. We are investigating whether treatment in the STaMINA clinical trial increases the chance of having no myeloma cancer cells detected by this method.

The results of the PRIMeR ancillary study will help investigators understand the results of the STaMINA clinical trial; and in the future will help in selecting the best treatment for patients with myeloma.

Your participation in the PRIMeR Ancillary Study will involve collection of three bone marrow samples in the course of one year (Figure 1). These samples will be kept at the BMT CTN Research Sample Repository. The first and third bone marrow samples will be collected as part of the scheduled evaluations in the STaMINA clinical trial and routine assessment of your disease. One additional bone marrow aspiration procedure will be done as part of the PRIMeR ancillary study. This additional procedure will be done prior to initiation of maintenance therapy in the STaMINA trial (see bold arrows in Figure 1 for when all PRIMeR bone marrow collections will happen).

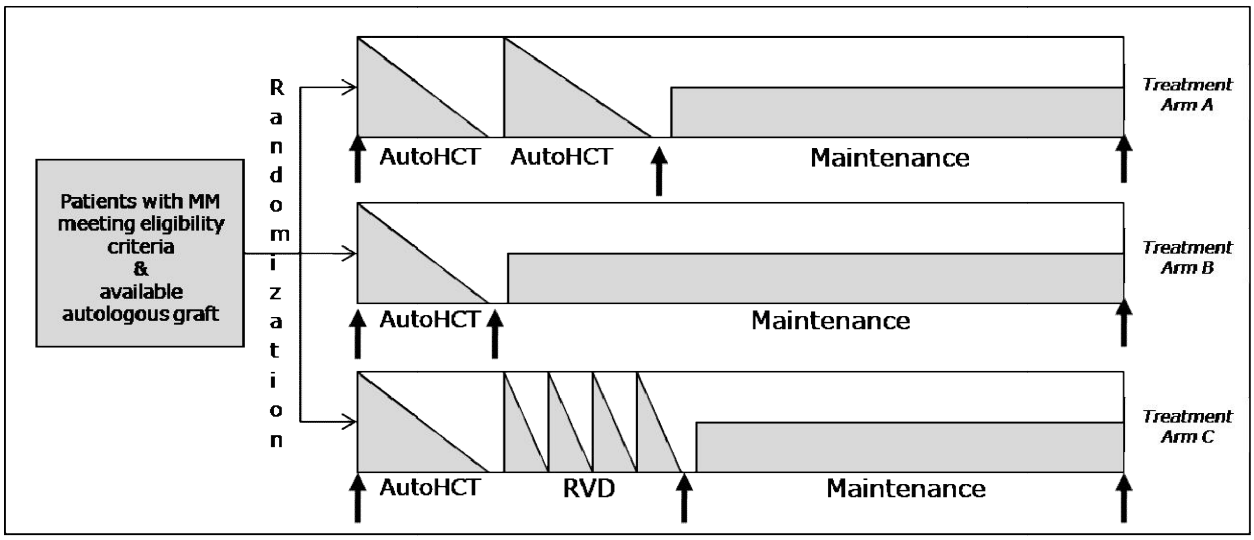

Figure 1 -- Outline of the STaMINA clinical trial. The arrows represent times that a bone marrow is collected as part of the PRIMeR study.

Some general things you should know about letting us store your bone marrow samples for research are:

- We will only store samples from people who give us permission. You should feel free to talk over your decision with your family, friends, doctor, and health care team. If you decide to not let us store research samples now or in the future, it will not affect your medical care.
- Research is meant to gain knowledge that may help people in the future. You will not get any direct benefit from taking part. Taking part may also involve some risks.
- All testing done on your blood and tissue samples are for research purposes. You or your doctor will not be given results and they will not be added to your medical record.
- You will not get paid for any samples or for any products that may be developed from current or future research.

If you agree to provide bone marrow samples, here is what will happen:

a.) Bone Marrow Aspirate Samples: if you have multiple myeloma, it is likely that you have already had a bone marrow biopsy and aspirate as part of your evaluations. Bone marrow tests are done as part of your routine medical care in case the multiple myeloma is not detected in blood or urine, in order to make sure your disease is in remission. Also, all patients in this study will have a bone marrow examination done prior to the first transplant. We are asking that an additional sample of the liquid bone marrow (2 teaspoons) be collected for research purposes. A small volume of liquid marrow (1/2 teaspoon) will be set aside for the PRIMeR ancillary study for three bone marrow aspirates collected in the first year of the study (PRIMeR Study Figure 1 above). After the first bone marrow examination, a maximum of 5 bone marrow examinations will be performed for research purposes, three in the first year and once a year thereafter (3 more times). Most, but not all, of these samples will be collected at the time that a bone marrow examination would be done anyway as part of your routine clinical care.

b.) All research samples will be given a unique bar code designation that cannot be linked to you by the researcher testing your samples.

c.) Researchers can apply to study the materials stored in the Repository.

d.) Materials stored in the Repository will be used mainly by clinicians and researchers in the BMT CTN network. In the future, the remaining research samples and clinical data will be made available outside of this network. Researchers from other universities, the government, and drug or health-related companies can apply to use the samples and information. Only skilled researchers will be allowed to use the samples and information.

e.) The BMT CTN Steering Committee or the BMT CTN Biomarkers Committee must approve each study application before they will share samples or information with researchers. This kind of review is to make sure that the investigators requesting the samples are qualified, and that the research they propose has a high potential of success and for contribution of scientific knowledge.

f.) DNA from your stored bone marrow samples might be used in genome-wide association (GWA) studies for a future project either done or supported by the National Institutes of Health (NIH).

If your coded samples are used in such a study, the researcher is required to add your test results and sample information into a shared, public research database. This public database is called the NIH Genotype and Phenotype Database and it is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you, or link you to your information or research samples.

Genome-wide association studies are a way for scientists to identify genes involved in human disease. This method searches the genome for small genetic changes that are more common in people with a particular disease than in people without the disease. Each study can look at hundreds of thousands of genetic changes at the same time. Researchers use data from this type of study to find genes that may add to a person's risk of developing a certain disease.

A new federal law (2009), called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Health insurance companies and group health plans must not request your genetic information that we get from this research. This means that they may not use your genetic information when making decisions regarding insurability. Be aware that this new federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

What if I am not eligible for the full research protocol?

If the Principal Investigator determines that you are not eligible for the research protocol your samples will not be used and will be discarded.

What if I change my mind?

You can change your mind about allowing us to use your samples and health information for research at any time. We ask that you contact [Principal Investigator] in writing and let him/her know you do not want us to use your research samples or health information for research. His/her mailing address is on the first page of this form. If you withdraw yourself from this protocol, even if you allowed your samples to be used for research, your samples will not be used from that point and they will be discarded. However, samples and information that have already been shared with other researchers cannot be taken back or destroyed.

HIPAA[1] authorization to use and disclose individual health information for research purposes

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of collecting bone marrow samples and information regarding the research study entitled *A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma.*

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment), physical examination findings, and laboratory test results obtained at the time of work-up and after transplantation (e.g., bone marrow tests, blood tests, biopsy results).

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from (*list hospitals, clinics or providers from which health care information can be requested*).

_____

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1 HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information.

d. Parties Who May Receive or Use My Individual Health Information: The individual health information disclosed by parties listed in item "c." above and information disclosed by me during the course of the research may be received and used by the following parties:

- Principal Investigator and the researcher's staff
- Dr. Amrita Krishnan, Study Chairperson and staff/laboratories at City of Hope National Medical Center
- Dr. George Somlo, Study Chairperson and staff/laboratories at City of Hope National Medical Center
- Dr. Edward Stadtmauer, Study Chairperson and staff/laboratories at University of Pennsylvania Cancer Center.
- National Heart, Lung, and Blood Institute (NHLBI) and National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN), data and coordinating center
- The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.
- The NCI-sponsored Cancer Cooperative Groups that enroll patients on this trial through the CTSU
- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments
- Celgene (the manufacturer of lenalidomide)
- Biologics, Inc. (the distributor of lenalidomide)
- Millennium Pharmaceutics (the manufacturer of Bortezomib)

e. Right to Refuse to sign this Authorization: I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research-related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

f. Right to Revoke: I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

g. Potential for Re-disclosure: My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer

protected. Examples include potential disclosures for law enforcement purposes, mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

h. This authorization does not have an expiration date.

PROBLEMS OR QUESTIONS

If you have questions about this study or experience a research-related injury, you should contact Dr. _____ at *insert phone number*. If you have any questions about your rights as a research participant, please contact _____ at *insert phone number*, or if you prefer, you can direct your questions to _____ at the following address: *insert address here*.

SIGNATURE PAGE

Statement of consent

The purpose of storing bone marrow samples for future research and/or for the PRIMeR study, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

I understand that I do not have to allow the use of my bone marrow samples for future research nor for the PRIMeR ancillary study. If I decide to not let you store future research and/or PRIMeR bone marrow samples, it will not affect my medical care in any way.

I voluntarily agree that my bone marrow samples and information can be stored indefinitely by the BMT CTN Repository for research to learn about, prevent, or treat health problems. I also understand that my DNA and health information may or may not be used in genome-wide association studies.

- ☐ I agree to allow my pre-transplant bone marrow samples to be stored and used for future research.
- ☐ I do not agree to allow my pre-transplant bone marrow samples to be stored nor used for future research.
- ☐ I agree to allow my pre-transplant bone marrow samples to be stored and used for the PRIMeR study.
- ☐ I do not agree to allow my pre-transplant bone marrow samples to be stored nor used for the PRIMeR study.

_____	_____	_____
Research Subject's Name *(Typed or printed)* **OR**	**Research Subject's Signature**	**Date**
_____	_____	_____
Research Subject's Legal Guardian/Representative *(Typed or printed)*	**Legal Guardian's Signature**	**Date**
_____	_____	_____
Witness's Name and Title *(A witness to the research subject's signature is required.)*	**Witness's Signature**	**Date**

Signature of person explaining and obtaining the consent:

_____	_____	_____
Name and title *(Typed or printed)*	**Signature**	**Date**

(Note: This consent form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the research subject. A copy should be placed in the research subject's medical record, if applicable.)

Informed Consent to Participate in Research

You are being asked to take part in a large clinical trials research study. About 750 patients will take part in this study at many centers around the country. Your participation in this study is expected to last an average of 4 years.

This consent form tells you about the study. The Principal Investigator (the person in charge of this research) or a co-worker of the Principal Investigator will also describe this study to you and answer all of your questions. Furthermore, throughout your treatment your care will be discussed with you and questions answered as needed. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. Taking part in this study is entirely your choice.

1. Name of the Subject ("Study Subject")

2. Title of Research Study

A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma

3a. Principal Investigator Contact Information

Insert name, affiliation and contact information.

3b. Contact information for emergencies after hours or on weekends or holidays

Call (###) ###-####, the in-patient Bone Marrow Transplant Unit. Ask to speak to the Charge Nurse.

4. Sponsor and Source of Funding or Other Material Support

The sponsor of this study, The National Institutes of Health (NIH), is providing financial support for the coordination of this study through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).

5. What is the purpose of this study?

You are being asked to take part in this research study because you have multiple myeloma (MM), a cancer of the bone marrow. The study described in this consent form is designed to test different treatment strategies for patients with multiple myeloma. Multiple myeloma is considered incurable. The standard therapy sometimes produces remission (absence of disease) in some individuals, but the disease recurs in all patients.

Past studies have shown that high-dose chemotherapy (drugs that kill cancer) can improve the survival of myeloma patients. However, this intensive therapy damages the special cells in the bone marrow called blood stem cells. Blood stem cells are cells found in the bone marrow and blood stream that produce all of the body's blood cells. Without healthy blood stem cells, a person cannot produce white blood cells (which fight infection), red blood cells (which transport oxygen to organs) or platelets (which help blood clot). Blood stem cells can be collected from the patient before high-dose chemotherapy. Then, after the patient receives high-dose chemotherapy these blood stem cells are returned intravenously (through a vein) to the patient. This procedure is called autologous **stem cell transplantation** (SCT). Autologous transplantation is accepted standard therapy for patients with multiple myeloma. Although high-dose chemotherapy with autologous SCT has significantly improved the survival of myeloma patients, it does not cure them and the potential to further improve treatment remains. One approach has been to kill myeloma cells left after the first autologous SCT with another course of high-dose therapy and a second autologous SCT. Studies have shown that receiving two autologous transplants a few months apart (tandem autologous SCT) improves survival for patients with multiple myeloma. Unfortunately, this approach still does not cure myeloma. It is not known if additional drugs given after the second autologous SCTs will further improve survival of patients with multiple myeloma. This study will test whether adding lower doses of drugs that are active against myeloma will prolong the survival by preventing the cancer cells to grow again. There are new drugs that have demonstrated significant activity against myeloma, they include lenalidomide and bortezomib. The study will assess whether adding these medications after the autologous SCT will improve the period the cancer stays inactive. There are two ways in which these drugs can be used after SCT. One approach is consolidation treatment and that has the same aim as a second autologous transplant that is to kill any leftover myeloma cells that remained after the first autologous transplantation. This study will evaluate whether this approach is superior to two (tandem) autologous SCT. The other approach is to assess whether maintenance therapy with low doses of continuous lenalidomide after an autologous SCT is better than the other two treatments described above (see picture). Maintenance treatment is designed to help the treatment succeed and is given to patients with cancer in remission to prevent progression. In summary, there are three main groups to be compared in this study: tandem autologous SCT + maintenance, one autologous SCT +

consolidation + maintenance and one autologous SCT + maintenance. The different treatments will be tested by randomizing patients to one of the three treatments before their first autologous SCT. Randomizing means assigning to a treatment by chance, like the flip of a coin.

In more detail, the consolidation treatment will include the combination of three drugs: lenalidomide, bortezomib and dexamethasone (or RVD) given for four cycles, each cycle being 21 days long. The maintenance uses lenalidomide alone continuously for a period of three years or until there is evidence that the cancer is becoming more active. This study will compare the time it takes for the disease to become active (progression-free survival) between the two single transplant arms and each single transplant arm to the tandem transplant arm. Additionally, this study will compare how the disease responds to each treatment given to you, specifically how the cancer responded after one year from entering the trial and yearly thereafter. For individuals who have not achieved maximum response (complete response) by the time they start maintenance, the rate of achieving maximum response during maintenance will be assessed and compared between treatment arms. Additional comparisons and assessment in this study include, overall survival, if a particular treatment prolongs more the survival than other treatments, assessment of the side effects of treatment, quality of life and incidence of infections in all three study treatments.

The study may find that patients who have different treatments for MM have similar results.

6. What will be done if you take part in this research study?

If you decide to take part in this study and have signed the informed consent, you will be evaluated to reduce the risk of having adverse events while participating in this study. Before starting treatment in this study, your doctor will check your general health.

You will have the following tests and evaluations to find out if you can participate:

- Medical history and physical examination, including height and weight.
- Blood tests (approximately 4 – 5 tablespoons).
- Urine tests.
- Electrocardiogram (ECG or EKG), a picture of the electrical action of the heart.
- Echocardiogram (a picture of the heart in motion made using ultrasound or sound waves) or MUGA scan (a picture of your heart after a small amount of radioactive material is injected into the bloodstream through a vein) to evaluate your heart function.
- Pulmonary Function Test (PFT), which is a breathing test that tells how your lungs are working, measures the amount of air taken into your lungs and exhaled as you breathe.
- Bone marrow biopsies and aspirates. A bone marrow aspiration is a procedure in which an area of the hipbone is numbed, and a small sample of bone marrow is withdrawn. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle.

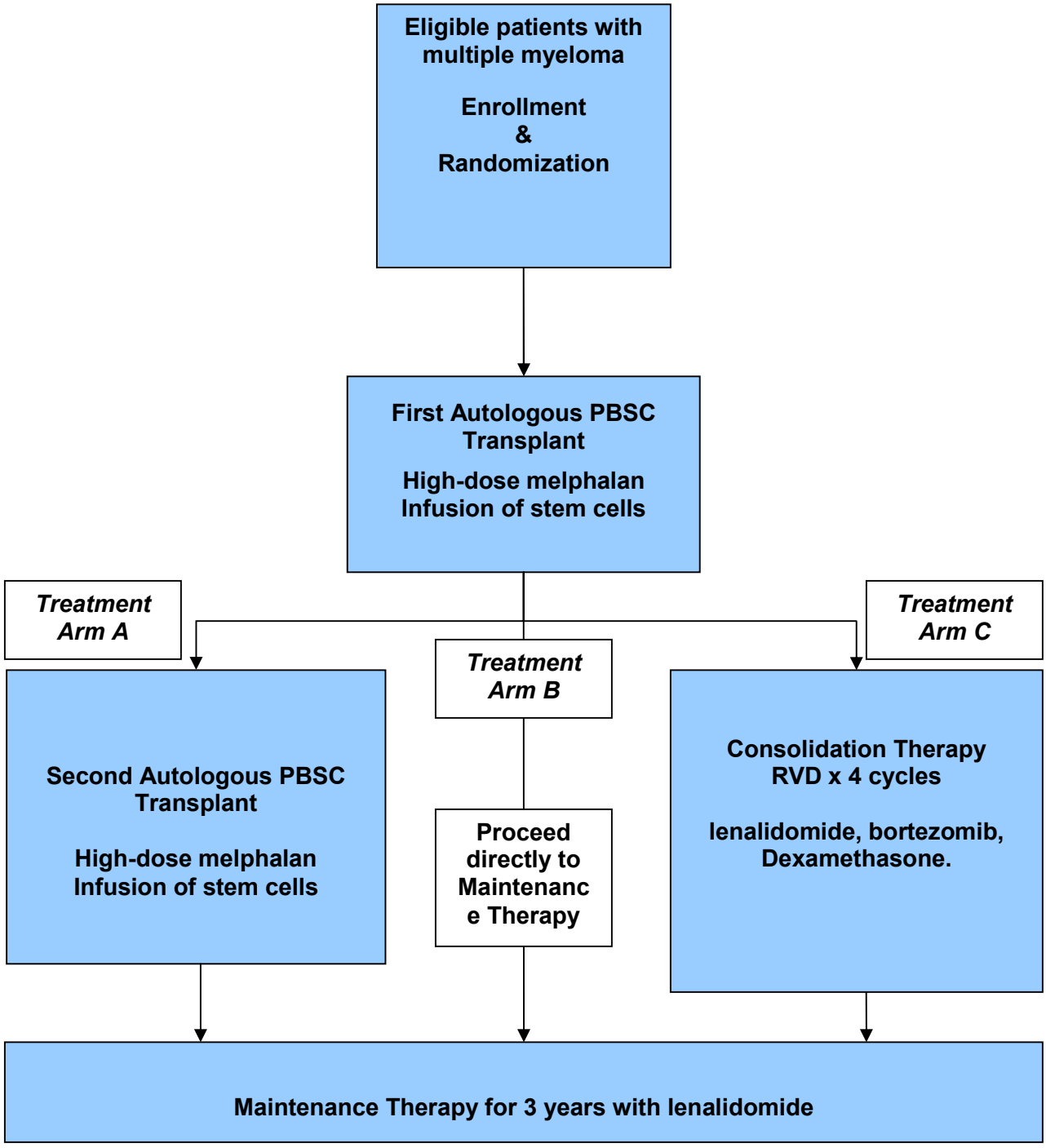
- If you are a woman able to have children, a serum pregnancy test will also be performed. If you are pregnant, you will not be able to take part in this study. Pregnancy tests will be repeated prior to and while you are taking lenalidomide. You must also commit to either continued abstinence from heterosexual intercourse or begin TWO acceptable methods of birth control, one highly effective method and one additional effective method AT THE SAME TIME, at least 4 weeks before she starts taking lenalidomide.
- If you are a man who has sexual relations with women who can become pregnant, you will be required to use a latex condom during sexual relations while taking lenalidomide.

Some additional x-rays will be done to evaluate your disease. These tests will help your doctor determine the amount of disease you have at the start of treatment and to follow the status of your disease throughout your treatment.

This study is divided into three phases and is explained in detail below. All patients will undergo the Phase I treatment portion of this study, using high-dose chemotherapy (melphalan) followed by an autologous SCT. Phase I is considered standard of care for patients with multiple myeloma, the research aspect of the study is the randomization in Phase II. Under the Phase II treatment portion of this study, you will be randomized (like the tossing of a coin) to one of three treatment arms. Patients randomized to receive a second autologous SCT (referred to as Treatment Arm A) will receive the same high-dose chemotherapy (melphalan) as described above followed by maintenance therapy with lenalidomide. Patients randomized to maintenance (Treatment Arm B) will receive maintenance therapy with lenalidomide after the first autologous transplantation. Patients randomized to consolidation and maintenance (Treatment Arm C) will receive consolidation therapy (bortezomib, lenalidomide and dexamethasone) followed by maintenance therapy with lenalidomide. Regardless of the treatment arm you are assigned, you will receive three years of maintenance lenalidomide. Your doctor will tell you your Treatment Arm placement.

One of the objectives of this study is to evaluate how the treatment affects the quality of the patient's life and whether there is a difference between the three treatment arms. Therefore, all English and Spanish speaking patients will be asked to complete questionnaires asking about their quality of life before the first and second transplants, prior to consolidation maintenance therapy and at one year from enrollment to the trial and yearly thereafter until four years from your enrollment in the study or until your disease returns or becomes active whichever comes first. It will take you approximately half an hour to complete the questionnaires.

Outline of Treatment Plan



Patient Initials _____

First Phase of the Study (All Study Participants)

Central Venous Catheter: You will need to have a central venous catheter (CVC) placed to participate in the study. A central venous catheter is a flexible sterile tube that will be placed into a large vein that runs under your collarbone so that blood can be withdrawn and medications given to you more easily and with less discomfort. This tube is usually placed under local anesthesia. There is a lot of experience with the use of these catheters. Complications include blood clots and infection. Clotting may require removal of the catheter or treatment of the clot by instilling a medicine that dissolves blood clots into the line. If you develop an infection you will require treatment with antibiotics and your catheter may need to be replaced. Other uncommon side effects may include swelling of the face and arm and/or lung collapse. If the lung collapses, it may be necessary to place a tube between the ribs to allow the lung to re-expand.

Mobilization and Leukapheresis (collection of stem cells from your peripheral blood), also called apheresis: There are several ways to collect stem cells for the SCT and the one selected depends on your doctor's preferences or the practice most commonly performed at your transplant center. This is not dictated as part of this protocol and it is routinely performed for all SCT. Briefly, the methods may involve administration of chemotherapy plus bone marrow stimulating medication, bone marrow stimulating cells alone or with other medications that help the release of stem cells from the bone marrow into the blood circulation (mobilization). This allows for collection of stem cells for the transplant through a central venous catheter (mentioned above) or a vein from your arm. If you receive chemotherapy as part of the mobilization, your doctor will explain the side effects, benefits and types of chemotherapy you may receive to mobilize your blood stem cells. Following chemotherapy for stem cell mobilization, you will receive a bone marrow stimulating medication called granulocyte-colony stimulating factor (G-CSF) by injection under your skin daily for approximately 10 days. G-CSF will help to move your stem cells out of the bone marrow into the bloodstream. You or someone who agrees to be responsible may be taught how to give you the G-CSF, so you can receive it at home. Once the number of stem cells in your blood stream is high enough, they will be collected over 2-5 days, while you are still receiving the G-CSF injections. A procedure called Leukapheresis will be done to collect your stem cells. During this procedure, your blood will be collected either through your central venous catheter or from a vein in one arm, processed through a machine to remove the white blood cells (stem cells), and then the rest of the blood will be returned to you through your catheter or a vein in the other arm. The leukapheresis procedure will last approximately several hours each time. **You will be asked to sign a separate consent form for the leukapheresis procedure.** Enough stem cells will be collected from you for two autologous SCTs. Your stem cells will be frozen (cryopreserved) until the time when they will be given back to you. Other methods to mobilize stem cells include only G-CSF, which follows the same description as above but without the chemotherapy. New medications have been approved for routine mobilization of stem cells, which if used will be explained to you by your doctor.

Measurements of Waist and Hip: During this study, your doctor or nurse will make measurements of your waist and hip. These measurements will be done at most three times during the study. This information will be collected and will be used along with your height and weight to study if they are related to the development of complications after the transplant.

Autologous Stem Cell Transplant: Approximately a couple of weeks after your stem cells have been collected, you will undergo an autologous SCT using high-dose chemotherapy with a drug called melphalan given through your central venous line. Since this high-dose treatment destroys the normal bone marrow in addition to the myeloma cells, your blood stem cells (blood cells able to mature and grow into useful part of your bone marrow such as red cells, white cells and platelets) must be given back to you. Your previously collected stem cells will be unfrozen and given back to you through your central venous catheter, similar to a blood transfusion, one or two days after you received the melphalan. Starting on the fifth day after you received your stem cells, you will be given the drug G-CSF, subcutaneously (under the skin) or intravenously (through a vein). G-CSF is called a growth factor and helps to stimulate the bone marrow to produce cells and will continue until your white blood count returns to normal.

Table 1 -- High-Dose Melphalan / Autologous SCT

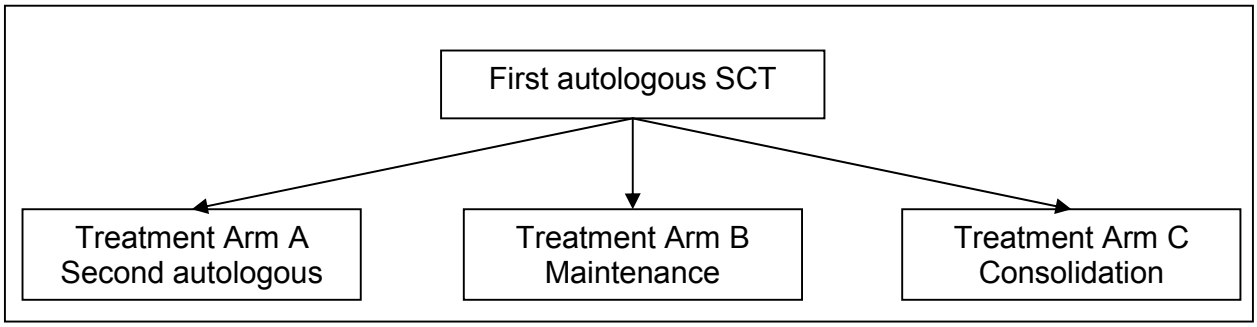
	-2 OR -1	**0**	**+5 or per Institutional Guidelines to Engraftment**
Melphalan	X		
PBSC Infusion		X	
G-CSF (5 μg/kg/day) SQ until ANC recovery (defined as an ANC ≥ 500/mm^3 x 2 days)			X

After your stem cells have been infused, it will take about two weeks before adequate numbers of blood cells are made. During this time you may not be making any of your own useful blood cells and therefore may require several red blood cell and platelet transfusions. Because your immune system is very weak, you may develop serious infections. You will be watched closely and receive antibiotics at the earliest sign of infection. During the time that your blood counts will be low, you may have mouth sores and feel very tired. You will receive medications to lessen these symptoms as much as possible. You will probably have a poor appetite during this time and may need to be given feedings through the central venous catheter. You may also receive pain medications as needed to minimize and control discomfort and pain. Once you begin to make new blood cells, the risk of serious infections will gradually be reduced. You should gradually come to the point where you will no longer require red cell and platelet transfusions. You should gradually regain your appetite. Although it is possible that the entire process may be done in the outpatient setting, it is also possible that a hospital stay of approximately 3 to 4 weeks will be necessary.

After completion of the transplant process, you will be followed in the outpatient clinic facility at least weekly, or as clinically indicated, until you are ready for your second intervention.

Second Phase Treatment Arms

Approximately 60 to 120 days after your initial autologous SCT, you will receive one of three therapies: a second autologous SCT, consolidation therapy, or maintenance.



Treatment Arm A (Second Autologous SCT)

If you are placed on Treatment Arm A, you will receive a second autologous transplant between 2 to 4 months from the initial transplant (this is usually the length of time it takes you to recover from your initial transplant). You will then receive maintenance therapy with lenalidomide (an anti-myeloma medication) at a dose of 10 mg daily for three months then the dose will be increased to 15 mg every day for a total of three years. Maintenance will starts 2 to 4 months after the second autologous transplant. You will also receive aspirin per your institution's guidelines during the lenalidomide maintenance.

You will be seen frequently in the clinic for evaluation. During the recovery from the first and second transplant you may be seen in clinic at least weekly. During maintenance you will be required to come to clinic once a month for the first three months and then every three thereafter. Evaluations may include physical exam, interview with a physician, blood and urine test, x-rays and if necessary a bone marrow biopsy in case there is no evidence of cancer elsewhere. You will require a blood test prior to the monthly supply of lenalidomide. These tests may be done remotely and sent to the transplant center.

Additional assessments: If you are a woman able to become pregnant you will undergo pregnancy counseling and test as long as you are taking lenalidomide. The test will be performed 10-14 days prior to starting lenalidomide, again within 24 hours of starting lenalidomide, weekly for the first four weeks of taking lenalidomide, and then every four weeks thereafter. If your periods are irregular, you will have additional serum pregnancy test performed at two weeks. An additional pregnancy test will be done 28 days after stop taking lenalidomide.

Treatment Arm B (Maintenance)

If you are placed on Treatment Arm B, you will start maintenance therapy with the drug, lenalidomide (an anti-myeloma medication) 2 to 4 months after the first and only transplant (this is usually the length of time it takes you to recover from your initial transplant). You will receive maintenance for a total of three years. The dose will start at a dose of 10 mg of lenalidomide every day for the first three months and it will be increased to 15 mg every day for a total of three years. You will also receive aspirin per your institution's guidelines during the lenalidomide maintenance.

You will be seen in the clinic at least weekly after the transplant. During maintenance you will be required to come to clinic once a month for the first three months and then every three thereafter. Evaluations may include physical exam, interview with a physician, blood and urine test, x-rays and if necessary a bone marrow biopsy in case there is no evidence of cancer elsewhere. You will require a blood test prior to the monthly supply of lenalidomide. These tests may be done remotely and sent to the transplant center.

Additional assessments: If you are a woman able to become pregnant you will undergo pregnancy counseling and test as long as you are taking lenalidomide. The test will be performed 10-14 days prior to starting lenalidomide, again within 24 hours of starting lenalidomide, weekly for the first four weeks of taking lenalidomide, and then every four weeks thereafter. If your periods are irregular, you will have additional serum pregnancy test performed at two weeks. An additional pregnancy test will be done 28 days after stop taking lenalidomide.

Treatment Arm C (Consolidation Therapy)

If you are placed on Treatment Arm C, you will receive consolidation therapy between 2 to 6 months after the initial transplant (this is usually the length of time it takes you to recover from your initial transplant). Consolidation therapy will consist of dexamethasone, lenalidomide, and bortezomib and this combination is also referred as RVD. You will be given consolidation therapy for a total of 4 cycles (where each cycle is 21 days long) with the combination bortezomib (1.3 mg/m^2 on Days 1, 4, 8 and 11 of each cycle), dexamethasone (40 mg total dose per day given on Days 1, 8, and 15 of each cycle) and lenalidomide (15 mg orally on Days 1-14 of each cycle). Bortezomib is administered either subcutaneously (under the skin) or intravenously (through the vein) as a rapid injection. The drugs used in consolidation treatment have the ability to cause blood clots, called deep vein thrombosis (DVT) if in the legs and pulmonary embolus (PE) if in the lungs. To try and prevent this from occurring you will be offered aspirin per your institution's guidelines during consolidation therapy unless you are treated with alternate prophylaxis of either heparin products or warfarin (Coumadin®).

Table 2 -- RVD Treatment Schedule

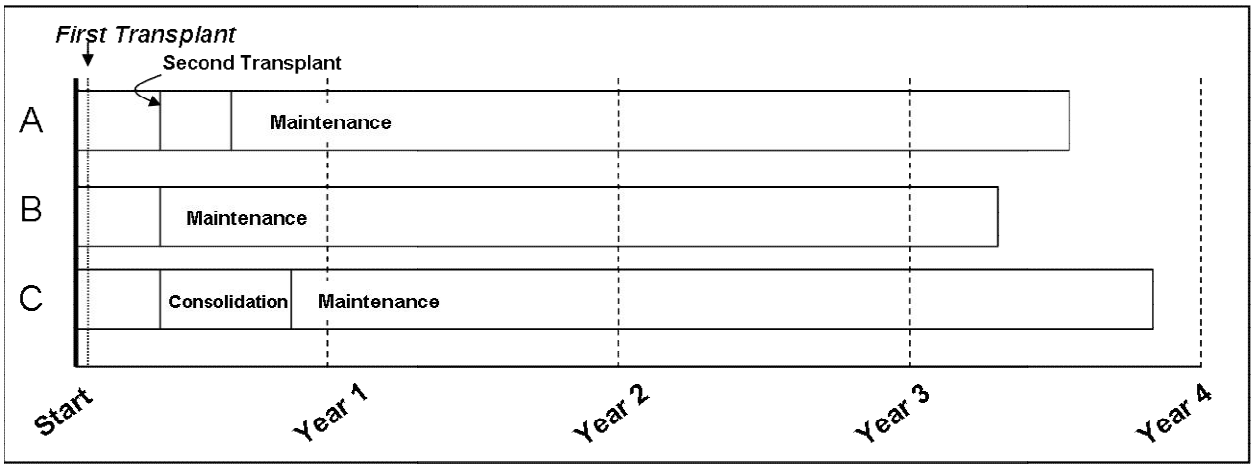
Dexamethasone	**40 mg Days 1, 8, 15**
Lenalidomide	**15 mg/day Days 1 to 14**
Bortezomib	**1.3 mg/m2 Days 1, 4, 8, 11**

You will receive maintenance therapy with the drug, lenalidomide (an anti-myeloma medication) 2 and a half to 6 months after the start date of consolidation therapy. The drug will be administered as 10 mg per day continuously for 3 months then increased to 15 mg daily. You will continue on lenalidomide maintenance for three years. You will also receive aspirin per your institution's guidelines during the lenalidomide maintenance.

You will be seen in the clinic at least weekly after the transplant. During maintenance you will be required to come to clinic once a month for the first three months and then every three thereafter. Evaluations may include physical exam, interview with a physician, blood and urine test, x-rays and if necessary a bone marrow biopsy in case there is no evidence of cancer elsewhere. You will require a blood test prior to the monthly supply of lenalidomide. These tests may be done remotely and sent to the transplant center.

Additional assessments: If you are a woman able to become pregnant you will undergo pregnancy counseling and test as long as you are taking lenalidomide. The test will be performed 10-14 days prior to starting lenalidomide, again within 24 hours of starting lenalidomide, weekly for the first four weeks of taking lenalidomide, and then every four weeks thereafter. If your periods are irregular, you will have additional serum pregnancy test performed at two weeks. An additional pregnancy test will be done 28 days after stop taking lenalidomide.

Outline of treatment arms A, B and C from enrollment (Start) to four years, demonstrating the length of each treatment arm.



7. Will You Provide Blood and Bone Marrow Samples for Research?

Researchers are trying to learn more about multiple myeloma and other health problems. Much of this research is done using human tissue or blood. These samples are collected during the clinical trial and stored for future use.

You are being asked to let us store some of your blood and bone marrow samples for use in future research and/or the PRIMeR (Prognostic Immunophenotyping in Myeloma Response) ancillary study. The collection for future research samples and the PRIMeR ancillary study samples can be doe at the same time.

Future Research Samples

Your blood and bone marrow samples for future research will be collected at your transplant center during the period you are participating in this study and kept at a central place called the BMT CTN Research Sample Repository (this will be called the "Repository" in the rest of the consent form). A Repository is a place that protects, stores and sends out samples for approved research studies.

Future research blood samples will be collected prior to the first autologous transplant, and prior to the initiation of maintenance therapy in all study arms. After initiation of maintenance, blood samples will be collected yearly throughout the course of the study (4 more times).

Future research bone marrow samples will be collected prior to first autologous transplant and yearly thereafter (4 more times). The bone marrow samples will be collected as part of the scheduled evaluations in the STaMINA clinical trial and routine assessment of your disease.

PRIMeR Ancillary Study Samples

The PRIMeR ancillary study will be conducted along with the STaMINA clinical trial. All patients who participated in the STaMINA clinical trial are eligible to participate in the PRIMeR ancillary study. This study will use a technique called flow cytometry to look for small quantities of myeloma cancer cells in your bone marrow. This method has been shown in

previous studies to help doctors predict which patients will have a longer period without their myeloma coming back. We are investigating whether treatment in the STaMINA clinical trial increases the chance of having no myeloma cancer cells detected by this method.

The results of the PRIMeR ancillary study will help investigators understand the results of the STaMINA clinical trial; and in the future will help in selecting the best treatment for patients with myeloma.

Your participation in the PRIMeR ancillary study will involve collection of three bone marrow samples in the course of one year (Figure 1). These samples will be kept at the BMT CTN Repository. The first and third bone marrow samples will be collected as part of the scheduled evaluations in the STaMINA clinical trial and routine assessment of your disease. One additional bone marrow aspiration procedure will be done as part of the PRIMeR ancillary study. This additional procedure will be done prior to initiation of maintenance therapy in the STaMINA trial (see bold arrows in Figure 1 for when all PRIMeR bone marrow aspirates will happen).

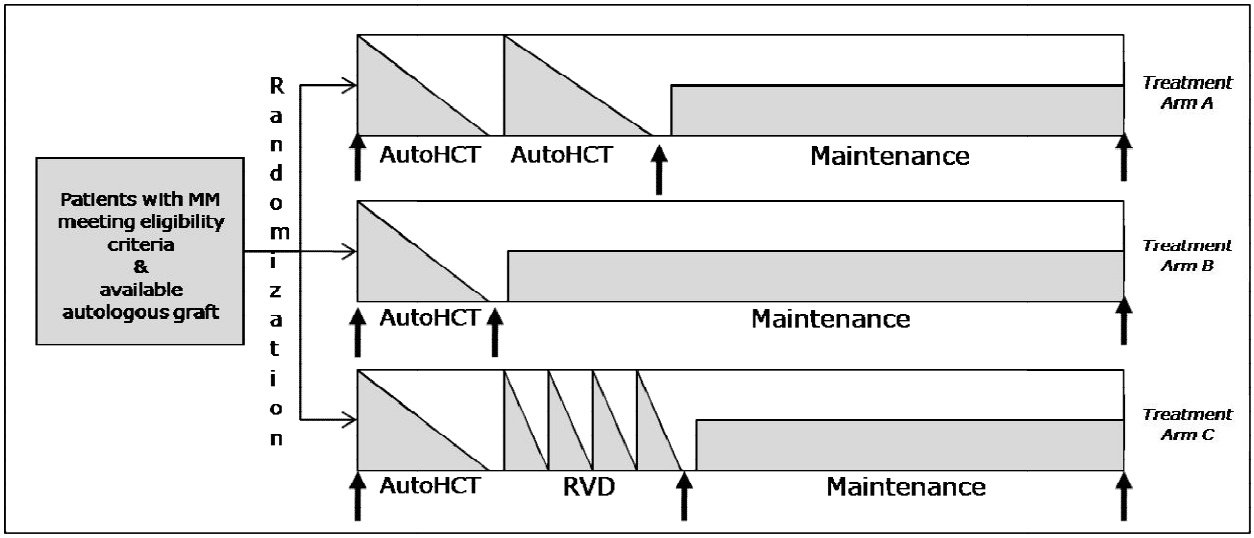


Figure 1 -- Outline of the STaMINA clinical trial. The arrows represent times that a bone marrow is collected as part of the PRIMeR study.

Some general things you should know about letting us store your blood and bone marrow samples for research are:

- We will only store samples from people who give us permission. You should feel free to talk over your decision with your family, friends, doctor, and health care team. If you decide to not let us store research samples now or in the future, it will not affect your medical care.
- Research is meant to gain knowledge that my help people in the future. You will not get any direct benefit from taking part. Taking part may also involve some risks.

- All testing done on your blood and tissue samples are for research purposes. You or your doctor will not be given results and they will not be added to your medical record.
- You will not get paid for any samples or for any products that may be developed from current or future research.

If you agree to provide blood and bone marrow samples, here is what will happen:

a) Blood Samples: a maximum of 20 samples of your blood (maximum of 6 teaspoons at each time) will be collected during the course of the study and stored solely for research purposes. The collections will be performed at the same time as the routine blood collections during the study.

b) Bone Marrow Aspirate Samples: if you have multiple myeloma, it is likely that you have already had a bone marrow biopsy and aspirate as part of your evaluations. Bone marrow tests are done as part of your routine medical care in case the multiple myeloma is not detected in blood or urine, in order to make sure your disease is in remission. Also, all patients in this study will have a bone marrow examination done prior to the first transplant. We are asking that an additional sample of the liquid bone marrow (2 teaspoons) be collected for research purposes. A small volume of liquid marrow (1/2 teaspoon) will be set aside for the PRIMeR ancillary study for three bone marrow aspirates collected in the first year of the study (PRIMeR Study Figure 1 above). After the first bone marrow examination, a maximum of 5 bone marrow examinations will be performed for research purposes, three in the first year and once a year thereafter (3 more times). Most, but not all, of these samples will be collected at the time that a bone marrow examination would be done anyway as part of your routine clinical care.

c) All research samples will be given a unique bar code designation that cannot be linked to you by the researcher testing your samples.

d) Researchers can apply to study the materials stored in the Repository.

e) Materials stored in the Repository will be used mainly by clinicians and researchers in the BMT CTN network. In the future, the remaining research samples and clinical data will be made available outside of this network. Researchers from other universities, the government, and drug or health-related companies can apply to use the samples and information. Only skilled researchers will be allowed to use the samples and information.

f) The BMT CTN Steering Committee or the BMT CTN Biomarkers Committee must approve each study application before they will share samples or information with researchers. This kind of review is to make sure that the investigators requesting the samples are qualified, and that the research they propose has a high potential of success and for contribution of scientific knowledge.

g) DNA from your stored blood or bone marrow samples might be used in genome-wide association (GWA) studies for a future project either done or supported by the National Institutes of Health (NIH).

If your coded samples are used in such a study, the researcher is required to add your test results and sample information into a shared, public research database. This

public database is called the NIH Genotype and Phenotype Database and it is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you, or link you to your information or research samples.

Genome-wide association studies are a way for scientists to identify genes involved in human disease. This method searches the genome for small genetic changes that are more common in people with a particular disease than in people without the disease. Each study can look at hundreds of thousands of genetic changes at the same time. Researchers use data from this type of study to find genes that may add to a person's risk of developing a certain disease.

A new federal law (2009), called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Health insurance companies and group health plans must not request your genetic information that we get from this research. This means that they may not use your genetic information when making decisions regarding insurability. Be aware that this new federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

What if I change my mind?

You can change your mind at any time about allowing us to use your samples and health information for research. We ask that you contact [Principal Investigator] in writing and let him/her know you do not want us to use your research samples or health information for research. His/her mailing address is on the first page of this form. If you withdraw yourself from this protocol, even if you allowed your samples to be used for research, your samples will not be used from that point and they will be discarded. However, samples and information that have already been shared with other researchers cannot be taken back or destroyed.

Statement of consent

The purpose of storing blood samples for future research, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

The purpose of storing bone marrow samples for future research and/or the PRIMeR study, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

I understand that I do not have to allow the use of my blood and/or bone marrow samples for future research. If I decide to not let you store research samples now or in the future, it will not affect my medical care in any way.

I understand that I do not have to allow the use of my bone marrow samples for the PRIMeR ancillary study. If I decide to not let you store bone marrow samples for the PRIMeR study, it will not affect my medical care in any way.

I voluntarily agree that my blood and/or bone marrow and information can be stored indefinitely by the BMT CTN Repository for research to learn about, prevent, or treat health problems. I also understand that my DNA and health information may or may not be used in genome-wide association studies.

- ❑ I agree to allow my blood to be stored for future research.
- ❑ I do not agree to allow my blood to be stored for future research.
- ❑ I agree to allow my bone marrow to be stored for future research.
- ❑ I do not agree to allow my bone marrow to be stored for future research.
- ❑ I agree to allow my bone marrow to be stored for the PRIMeR study.
- ❑ I do not agree to allow my bone marrow to be stored for the PRIMeR study.

_____ _____

Signature Date

8. What are the possible discomforts and risks?

The treatment used in this study may cause all, some, or none of the side effects listed below. Also, there is always the chance of unexpected new side effects.

ALL PATIENTS

G-CSF: G-CSF may cause local pain and burning at the injection site and some patients experience pain in their bone when treated with this drug. The bone pain is generally mild to moderate in severity and controllable in most patients with oral medication. The growth factor may cause your white count to become very high, which could affect your blood flow. Your white blood cell count will be measured, and if it becomes too high, the dose of the growth factor will be reduced or stopped. G-CSF may cause fluid retention and low blood pressure. Less common possible side effects include headaches, body aches, upset stomach, skin rash, fatigue and trouble sleeping. Other possible side effects are increases in uric acid, LDH, alkaline phosphatase and leukocyte alkaline phosphatase when given with cytotoxic drugs. Local inflammation and rarely an infection at the G-CSF injection site may also occur. Rarely your spleen can burst (called splenic rupture). Please let your doctor or healthcare provider know immediately if you experience any pain in the left upper stomach area or left shoulder tip. This may be a sign of enlarged or burst spleen.

Leukapheresis (collection of stem cells from your peripheral blood), also called apheresis: If you have a central venous catheter, this procedure will be done through the catheter and not through a vein. If done through a vein, the needle insertion used for the leukapheresis procedure may cause local bruising and infection in the vein or on the skin around the vein. The bruising resolves on its own and has no additional risks. The infection in the vein or of the skin around the vein would be treated with antibiotics.

Your blood will be thinned with citrate during the leukapheresis procedure. Citrate decreases the calcium in the blood sometimes causing temporary numbness or tingling of the fingertips or around the mouth. Should you experience any numbness, you must tell the nurse operating the machine. You will be given a dose of calcium to reverse this side effect, before the problem becomes severe. Other possible side effects of the collection procedure include lightheadedness, nausea or more rarely, fainting due to temporary lowering of the blood pressure. Stopping the procedure and giving additional intravenous fluids can correct this. Occasionally, the filtering process also removes platelets (the cells that help the blood to clot). If your platelet count falls low enough to place you in danger of bleeding, any further collection will be postponed until a replacement transfusion is given.

Blood Drawing: The risks of drawing blood from a vein include discomfort at the site of puncture (where the needle is placed in the vein); possible bruising and swelling around the puncture site; rarely, an infection; and uncommonly, faintness from the procedure. If you have a central line or catheter, these risks will not apply to you and the risks of the central line were explained to you at the time you had the line or catheter placed. Occasionally even if you have a central catheter, you may require blood draws from a vein requiring a needle stick.

Bone Marrow Aspiration and Biopsy: A bone marrow aspiration is a procedure in which an area of the hip (buttock area) is numbed with local anesthetic, and a small sample of bone marrow is withdrawn. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle. When the local anesthesia is given, you may initially feel a burning sensation in your skin and bone surface for several seconds. During the actual procedure itself, you may temporarily feel pressure and/or pain of varying degrees. If necessary, you may ask your physician for additional local anesthesia or a medication to ease your stress. You also may experience bleeding, and/or bruising after the procedure is completed and you may experience soreness in the area for a few days afterwards. Rarely an infection can develop.

Bone marrow aspirates and biopsies will be used to check how your disease is responding to the study treatments.

Unexpected Organ Damage and Other Side Effects: Although your major organs function well, it is possible that unexpected heart, lung, kidney, or liver damage may occur as a result of this therapy, which is rarely life-threatening and usually reversible with treatment. You will be informed if problems arise and the measures being taken to help you. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal despite intensive medical management. Other unpredictable side effects can occur and will be explained to you and treated by your physicians should unforeseeable problems arise.

Late Effects: These may include gland problems resulting in poor growth and sterility. There may be poor function of the thyroid gland, requiring thyroid hormone supplementation. There is also a risk of second cancers as a result of the chemotherapy and/or underlying disease. The risk of developing and dying from a secondary cancer is far less than the risk of dying from your disease without treatment. The long-term effects upon heart, lung, and brain are unknown.

Risk to the Unborn: The treatments in this study have not been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who have the potential of becoming pregnant must use some effective method of birth control. Effective birth control would be defined as the following: 1) refraining from all acts of vaginal intercourse (ABSTINENCE); 2) consistent use of birth control pills; 3) injectable birth control methods (Depo-Provera, Norplant); 4) tubal sterilization or male partner who has undergone a vasectomy; must still use latex condom; 5) placement of an IUD (intrauterine device); and, 6) use, with every act of intercourse, of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam.

Both men and women will be included in this study. Because the drugs in this study may affect an unborn baby, you should not become pregnant or father a baby while in this study. You must use a highly effective birth control method or a combination of 2 additionally effective birth control methods while in this study. The effect of bortezomib and lenalidomide on reproduction and its safety in pregnancy are unknown. If you are a woman capable of becoming pregnant [women that have not undergone a hysterectomy (removal of the womb), have not had both ovaries removed or have not been post-menopausal (stopped menstrual periods) for more than 24 months in a row], you must have a negative pregnancy test before beginning treatment. In addition, you must not be breastfeeding a baby during this study.

If you think that you have become pregnant or may have fathered a child while taking part in this study you must tell the study doctor immediately. The study doctor will advise you of the possible risks to your unborn baby and discuss options for managing the pregnancy with you. You should also notify the doctor managing your pregnancy that the mother/father received a study drug (name of study drug or drugs).

If you are a female study subject and you become pregnant during your participation in this study, your treatment with study drug will be stopped and you may be withdrawn from some of the study procedures but not from follow-up by your study doctor. The study doctor will ask for your permission to stay in contact with you throughout the length of the pregnancy.

If you are a male study subject and your partner becomes pregnant, the study doctor will ask for your partner's permission to collect information about her pregnancy and the health of the baby.

Laboratory tests show that bortezomib and lenalidomide may damage DNA. Based on this information, it is possible that bortezomib and lenalidomide may cause infertility in men and women (not being able to become pregnant or father a child).

Sterility and Future Childbearing Potential for Men and Women: Chemotherapy and /or irradiation may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use some effective method of birth control. Damage to reproductive tissue may result in birth defects or permanent inability to father a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

Therapy Toxicities: Unknown Toxicities may occur in any individual patient due to multiple events and cumulative effects, which may involve any and all organs, including the brain.

AUTOLOGOUS STEM CELL TRANSPLANT

Melphalan: The most common side effect in patients who have received melphalan has been nausea and vomiting (mild to moderate), loss of appetite (mild), diarrhea and skin rash. Your doctor will prescribe drugs to prevent and lessen these side effects should they occur. Melphalan will irritate your skin if it leaks outside of the vein while being given. Let your doctor or nurse know if you feel any burning, stinging or pain while you are receiving this drug. Notify your doctor right away if the area around the injection becomes red or swollen after you receive the drug. Side effects that occur several days or a week later include low blood count, mouth sores, temporary hair loss, fatigue and poor appetite. You may need blood and platelet transfusions while your counts are low and/or antibiotics to fight infections. Mouth sores which sometimes extend into the throat or esophagus can be painful, and some patients may require 7 to 10 days of morphine or a similar medication to control the discomfort. Mouth sores can also make eating difficult. If this occurs, patients will receive their nutrition intravenously until the problem resolves. In rare instances, melphalan can cause lung damage or a secondary cancer (a cancer caused by prior cancer treatment). Secondary cancers are often very difficult to treat and can be fatal.

Infusion of Autologous Stem Cells: The stem cell infusion is given similar to a blood transfusion. It is given through your central venous catheter. You will be given pre-medications just prior to the infusion to decrease the risk of a reaction. There is a very slight risk of infection due to contamination of the stem cell products during their storage or drawing. Some patients react to the preservative called DMSO, which is used in the freezing process of your stem cells. You may notice a garlic taste or smell from the DMSO. Common, less serious reactions for patients receiving an autologous SCT include mild wheezing, mild shortness of breath, back or chest pain or lightheadedness. In rare instances, a severe allergic reaction called anaphylaxis can occur leading to a drop in blood pressure or extreme difficulty in breathing. You will be monitored very closely during the infusion and afterwards to look for these reactions and given medications and/or intravenous fluids to correct these side effects. These complications are reversible with treatment.

Risk of Infection and Other Complications of Low Blood Counts: After any of the therapies in this study, but before the stem cells have begun to make new blood cells, your ability to fight infections will be very low. During that time you will be very susceptible to serious infections and will need to take extra precautions to limit your exposure to infectious agents. Bacteria, fungi and viruses that can easily be destroyed by a healthy person's immune system can cause a serious, and sometimes fatal, infection in patients with low white blood cell counts. You will be given medications to prevent infections and to treat them if you develop one as determined by your doctor.

After transplantation you may not be able to make red blood cells or platelets for approximately two to three weeks until the stem cells start growing in your bone marrow. If your red blood cell count is very low, you may have severe fatigue or shortness of breath. If your platelet count is low, there is a small chance of serious bleeding. Therefore, you may need red blood cell and platelet transfusions.

The risk of dying from the complications of an autologous transplant is less than 5%. This means that for every hundred patients who have an autologous transplant for multiple myeloma, up to 5 of them may die from complications of the treatment. It is not possible to know before your transplant if you will die from complications of treatment.

CONSOLIDATION THERAPY

Dexamethasone: This medication may temporarily increase blood pressure and blood sugar levels. Some patients require medication to control their blood sugar. Steroid medications have also been known to cause insomnia (difficulty sleeping), personality changes and depression. Dexamethasone may also cause nausea, vomiting, increased appetite, stretch marks, weight gain, fluid retention, swelling, gas and heartburn. These symptoms usually go away once the medication is stopped. Gas and heartburn can be treated with medications. Call your doctor if you experience these symptoms. Dexamethasone can also cause inflammation of the pancreas, pain, thinning and weakening of the bones, and the potential for a hip replacement.

Bortezomib: Bortezomib is also called **Velcade®.** Bortezomib should not be taken if you have ever had a serious allergic reaction to bortezomib, boron, or mannitol. You face some risks or

discomforts when you are treated with the study drug, bortezomib. You are at risk of having all, some, or none of these symptoms and they may vary in severity. The severity may be mild, moderate or severe, up to and including death. Any symptoms or conditions that you have before you start study drug may get worse. Also, there is always a chance that a risk that is rare or not yet known may occur. If any of these symptoms occur, you must tell your doctor who may give you other drugs to ease discomforts you have. Your doctor may lower or withhold the dose of bortezomib. Also, if you have a very bad reaction to the study drug, your doctor may permanently stop the study treatment for good.

Certain drugs or compounds may change the effectiveness of bortezomib, including grapefruit juice, green tea, vitamin C, and St. John's Wort. Call your doctor if you have questions about drug interactions.

Likely Side Effects (may occur in 20% of patients or more)	**Less Likely Side Effects (may occur in <20% of patients or less)**	**Rare Side Effects (can occur in less than 3% of patients)**
• Decrease in a red blood cell protein that carries oxygen in the body • Decreased number of blood cells that help to clot the blood • Infection which occurs due to a decreased number of a type of white blood cell • Fatigue • Fever in the absence on neutropenia • Anorexia • Loss of appetite • Constipation • Diarrhea • Nausea • Vomiting • Swelling of the arms and legs • Nerve damage causing numbness, tingling, burning	• Decreased total number of white blood cell • Decreased number of a type of white blood cell • Low blood pressure • Difficulty sleeping or falling asleep • Rigors/Chills, Rash/desquamation • Dehydration • Low blood pressure • Abnormal heart beat • Irritation or sores in the lining of the mouth or throat • Sore throat • Heartburn, dyspepsia • Ileus (functional obstruction of the bowel, i.e., neuroconstipation) • Mucositis/stomatitis • Hemorrhage (GI, pulmonary/upper respiratory) • Fever with dangerously low white blood cell count • Infection with low white blood cell count • Pneumonia • Opportunistic infection • Dizziness • Confusion • Anxiety • Changes in the way things taste • Abnormal liver tests • numbness, tingling, burning • Fainting • Blurred vision • Inflammation of the eye	• A hole in the digestive tract • Syndrome associated with high blood pressure characterized by headache, confusion, seizures, and vision loss associated with imaging findings • Kidney failure • Reversible posterior leukoencephalopathy syndrome (affects the brain and may cause headaches, changes in your vision, changes in your mental status, or seizures)

Likely Side Effects (may occur in more than 20% of patients)	Less Likely Side Effects (may occur in 20% of patients or less)	Rare Side Effects (can occur in less than 3% of patients)
	• Muscle weakness • Nerve damage • Fainting • Blurred vision • Belly pain • Back pain • Bone pain • Leg pain • Head pain • Joint pain • Muscle pain • Nerve pain • Cough • Shortness of breath • Excess fluid that accumulates in the pleural cavity, the fluid-filled space that surrounds the lungs	

Lenalidomide: This medication may cause skin rash, drowsiness or sleepiness, dizziness, confusion, tremor, loss of coordination, weakness, and numbness. Lenalidomide may also cause constipation, nausea, diarrhea, vomiting and inflammation of the mucosa of the mouth. General symptoms from taking this drug are weakness, weight loss, and fever. Lenalidomide can cause a significant increased risk of blood clot in multiple myeloma patients. Also this drug can cause a significant decrease in white blood cells (neutrophils) and platelets in the blood. Call your doctor if you experience these symptoms (see below under maintenance additional information about lenalidomide).

Reproductive Risks: Lenalidomide is known to be very harmful to fetuses and can produce miscarriages in pregnant women. It can cause severe life-threatening human birth defects or fetal death. Therefore it is very important not to be pregnant or become pregnant while on lenalidomide. All women of childbearing ages will receive pregnancy tests 10-14 days and 24 hours before starting this drug. Also pregnancy tests will be frequently administered while taking this drug and at the discontinuation of your therapy of this drug.

Because of the severity of these abnormalities, it is extremely important that pregnancies do not occur while you are taking lenalidomide.

You should discuss with your doctor what the best methods of birth control are for you. Remember, however, than no method of birth control besides complete abstinence provides 100% protection from pregnancy.

If you are a female patient taking lenalidomide, you must either abstain from all reproductive sexual intercourse or use two methods of birth control or at least one highly active method (e.g., intrauterine device [IUD], hormonal [birth control pills, injections or implants], tubal ligation, or partner's vasectomy) and one additional effective method (e.g., latex condom, diaphragm, or cervical cap), for at least 28 days before starting lenalidomide therapy, during therapy, and for at least 28 days after discontinuing lenalidomide therapy even when there has been a history of infertility, unless due to hysterectomy or because you have been post-menopausal or have had no menses (that is no menstrual period) for at least 24 continuous months.

Patients with multiple myeloma who take lenalidomide and dexamethasone have a greater chance of having blood clots. Because of this, it is recommended patients not take birth control pills or hormone replacement therapy before discussing with the doctor and considering the risks and benefits of these choices.

If you are a male patient, you will be counseled that lenalidomide may be present in your semen. You must use a latex condom every time you have sexual intercourse with a woman during therapy and for four weeks after discontinuing lenalidomide, even if you have had a successful vasectomy. You should request that female partners use a second method of birth control in addition to using a male condom.

Patients should not donate blood during study treatment or for 28 days following discontinuation of lenalidomide.

You will be counseled at least every 28 days either by counselors at the site or through the Revlimid REMS® program during lenalidomide treatment and again one last time when you stop taking lenalidomide about not sharing lenalidomide (or other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies" with each new supply of lenalidomide as a reminder of these safety issues.

MAINTENANCE THERAPY

Lenalidomide: Lenalidomide is also called **Revlimid®.** This medication may cause skin rashes, drowsiness or sleepiness, dizziness, confusion, tremor, loss of coordination, weakness, and numbness. Lenalidomide may also cause constipation, nausea, diarrhea, vomiting and inflammation of the mucosa of the mouth. General symptoms from taking this drug are weakness, weight loss, and fever. Lenalidomide can cause a significant increased risk of blood clot in multiple myeloma patients. Also this drug can cause a significant decrease in white blood cells (neutrophils) and platelets in the blood. Call your doctor if you experience these symptoms.

Sometimes a second cancer arises after patients have undergone cancer therapy, including chemotherapy used prior to autologous transplants. Recently, in clinical trials of patients with multiple myeloma, a higher number of second cancers has also been reported in patients treated with chemotherapy and/or autologous transplant followed by maintenance lenalidomide compared to those who did not receive lenalidomide.

We do not know at this time whether prolonged lenalidomide therapy in this clinical setting actually increases the risk of second cancers. No increase in second cancers has been observed in patients receiving lenalidomide therapy for other indications or for relapsed multiple myeloma.

We are carefully monitoring these events (second cancers) in all on-going studies of lenalidomide therapy. You will be given any new information regarding second cancers that might affect your decision to stay in the study.

Likely Side Effects (may occur in more than 20% of patients)	**Less Likely Side Effects (may occur in 20% of patients or less)**	**Rare Side Effects (can occur in less than 3% of patients)**
• Decreased number of a type of white blood cells (neutrophil/ granulocyte) • Decreased number of blood cells (platelets) that help to clot blood • Fatigue or tiredness • Anemia or decrease in a red blood cell protein (hemoglobin) that carries oxygen in the body • Constipation • Diarrhea •	• Decrease of the total number of white blood cells (leukocytes) • Decreased number of a type of white blood cell (lymphocyte) • Fever • Difficulty sleeping or falling asleep • Chills, shivering • Excessive sweating • Weight loss • A chronic, inflammatory skin condition with sores covering the skin • Abnormally low level of thyroid gland hormone • Loss of appetite • Irritation or sores in the lining of the anus • Irritation or sores in the lining of the mouth • Irritation or sores in the lining of the rectum • Irritation or sores of the lining of the small bowel • Vomiting	• Inflammation (swelling and redness) of the pancreas • Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness • Increased blood level of fat-digesting enzyme (lipase) • Group of signs and symptoms due to rapid breakdown of tumor that can occur after treatment of cancer has started that causes increased levels of blood calcium, potassium, uric acid, phosphate, and kidney failure • Temporary growth in tumor or worsening of tumor related problems • Progressive necrosis (tissue death) of a part (the white matter) of the brain

Likely Side Effects (may occur in more than 20% of patients)	Less Likely Side Effects (may occur in 20% of patients or less)	Rare Side Effects (can occur in less than 3% of patients)
	• Infection(s) somewhere in the body • Swelling of the arms and legs • Dizziness (or sensation of lightheadedness, unsteadiness, giddiness, spinning or rocking) • Belly pain • Back pain • Head pain or headache • Joint pain • Muscle pain • Cough • Shortness of breath • Formation or presence of a blood clot that breaks loose and is carried by the blood stream to plug another blood vessel • Itching • Rash with the presence of macules (flat discolored area) and papules (raised bump)/flaking or shedding of outer layer of skin • Nausea; the urge to vomit	without inflammation (swelling and redness) • Sudden or traumatic injury to the kidney • Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue • Potentially life-threatening condition affecting less than 10% of the skin in which cell death causes the epidermis (outer layer) to separate from the dermis (middle layer) • Life-threatening condition affecting greater than 30% of the skin in which cell death causes the epidermis (outer layer) to separate from the dermis (middle layer)

Because of the severity of these abnormalities, it is extremely important that pregnancies do not occur while you are taking lenalidomide.

You should discuss with your doctor what the best methods of birth control are for you. Remember, however, than no method of birth control besides complete abstinence provides 100% protection from pregnancy.

If you are a female patient taking lenalidomide, you must either abstain from all reproductive sexual intercourse or use two methods of birth control or at least one highly active method (e.g., intrauterine device [IUD], hormonal [birth control pills, injections or implants], tubal ligation, or partner's vasectomy) and one additional effective method (e.g., latex condom, diaphragm, or cervical cap), for at least 28 days before starting lenalidomide therapy, during therapy, and for at least 28 days after discontinuing lenalidomide therapy even when there has been a history of

infertility, unless due to hysterectomy or because you have been post-menopausal or have had no menses (that is no menstrual period) for at least 24 continuous months.

Patients with multiple myeloma who take lenalidomide and dexamethasone have a greater chance of having blood clots. Because of this, it is recommended patients not take birth control pills or hormone replacement therapy before discussing with the doctor and considering the risks and benefits of these choices.

If you are a male patient, you will be counseled that lenalidomide may be present in your semen. You must use a latex condom every time you have sexual intercourse with a woman during therapy and for 28 days after discontinuing lenalidomide, even if you have had a successful vasectomy. You should request that female partners use a second method of birth control in addition to using a male condom.

Patients should not donate blood during study treatment or for 28 days following discontinuation of lenalidomide.
Lenalidomide will be provided to you free of charge. Lenalidomide distribution for this trial will change from obtaining the drug directly through the transplant center to mail distribution directly to your address. The way you will be counseled will change due to the change in drug distribution.

You will be counseled at least every 28 days either by counselors at the site or through the Revlimid REMS® program during lenalidomide treatment and again one last time when you stop taking lenalidomide about not sharing lenalidomide (or other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies" with each new supply of lenalidomide as a reminder of these safety issues.

If you have ever received lenalidomide before, you are already registered in the Revlimid REMS® and there is no additional registration required for this clinical trial. If you have never received lenalidomide before, you will need to be registered in the Revlimid REMS®. This program is a controlled prescription mechanism to dispense lenalidomide for any indication. The registration involves a separate consent process, which outlines the reproductive risks related to this medication, and identifies you as a participant with this clinical trial. Information that will be required for consent includes your name, address, phone number, date of birth, and social security number. This information will be provided to Celgene Corporation and Biologics Incorporated to identify your registration in participating in this trial. RevAssist is the mandatory mechanism by the US Food and Drug Administration for dispending lenalidomide.

Any unused lenalidomide should be returned as instructed though the Revlimid REMS® program.

Additional Instruction for Taking Lenalidomide

Swallow lenalidomide capsules whole with water at the same time each day. Do not break, chew or open the capsules.

If you miss a dose of lenalidomide, take it as soon as you remember on the same day. If you miss taking your dose for the entire day, take your regular dose the next scheduled day (do NOT take double your regular dose to make up for the missed dose).

If you take more than the prescribed dose of lenalidomide you should seek emergency medical care if needed and contact study staff immediately.

Females of childbearing potential that might be caring for you should not touch the lenalidomide capsules or bottles unless they are wearing gloves.

Only one cycle of therapy will be provided to you each month through the Revlimid REMS® program. During maintenance a maximum of a 28-day supply will be dispensed.

Pregnancy:

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Preliminary findings from a monkey study appear to indicate that lenalidomide caused birth defects in the offspring of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby. Because of this risk, all patients taking lenalidomide must read the following statements that apply to them according to gender and menopausal status.

FOR FEMALES WHO *ARE ABLE* TO BECOME PREGNANT*

*(Sexually mature female who: 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries); or, 2) has not been naturally postmenopausal for at least 24 consecutive months)

Please read thoroughly and initial each space provided if you understand each statement

_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that my unborn baby may have birth defects and can even die, if I am pregnant or become pregnant while I am taking lenalidomide.

_____: I understand that I must NOT take lenalidomide if I am pregnant, breast-feeding a baby or able to get pregnant and not using 2 reliable methods of birth control.

_____: If I am having sexual relations with a man, my uterus and/or both ovaries have not been removed, I have had at least one menstrual period in the past 24 months and/or my menses stopped due to treatment of my disease, I understand that I am able to become pregnant. I must use one highly effective method of birth control plus one additional effective method of birth control (contraception) at the SAME TIME.

Highly Effective Methods	Additional Effective Methods
Intrauterine device (IUD)	Latex condom
Hormonal (birth control pills, injections, implants)	Diaphragm
Tubal ligation	Cervical Cap
Partner's vasectomy	

_____: These birth control methods must be used during the following time periods related to this study: 1) for at least 28 days before starting lenalidomide therapy; 2) while participating in the study; during interruptions in therapy; and, 3) for at least 28 days after lenalidomide has been stopped. I must use these methods unless I completely abstain from heterosexual sexual contact. If a hormone (birth control pill, injection, patch or implant) or IUD method is not medically possible for me, I may use another highly effective method or two barrier methods AT THE SAME TIME.

_____: I know I must have a pregnancy test done by my doctor within 10 – 14 days and again within 24 hours prior to starting lenalidomide therapy, even if I have not had my menses due to treatment of my disease or had as little as one menstrual period in the past 24 months. If I have regular or no menstrual cycles, I will then have pregnancy tests every week for the first 28 days, then every 28 days while I am taking lenalidomide, again when I have been taken off of lenalidomide therapy and then 28 days after I have stopped taking lenalidomide. If I have irregular menstrual cycles, I will have pregnancy tests every week for the first 28 days, then every 14 days while I am taking lenalidomide, again when I have been taken off of lenalidomide therapy, and then 14 days and 28 days after I have stopped taking lenalidomide.

_____: I know I must immediately stop taking lenalidomide and inform my doctor, if I become pregnant while taking the drug, if I miss my menstrual period or have unusual menstrual bleeding, if I stop using two reliable forms of birth control, or if I think for any reason that I may be pregnant. I must talk to my doctor before changing any birth control methods.

_____: I am not now pregnant, nor will I try to become pregnant for at least 28 days after I have completely finished taking lenalidomide.

_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children.

_____: I agree any unused drug supply will be returned as instructed through the Revlimid REMS® Program.

_____: I know that I cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.

Study patients who become pregnant will be monitored throughout the pregnancy and will continue to be monitored for 30 days after delivery (premature delivery, aborted fetus, full-term pregnancy, or no longer pregnant).

FOR ALL MALES

Please read thoroughly and initial each space provided if you understand each statement:

_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.

_____: I have been told by my doctor that I must NEVER have unprotected sexual contact with a female who can become pregnant. Because it is not known whether lenalidomide is present in semen, my doctor has explained that I must completely abstain from sexual contact with females who are pregnant or able to become pregnant, or I must use a latex condom every time I engage in any sexual contact with females who are pregnant or may become pregnant AND insist that my partners use highly effective contraception. I must do this while I am taking lenalidomide and for 28 days after I stop taking lenalidomide, even if I have had a successful vasectomy.

_____: I know I must inform my doctor if I have unprotected sexual contact with a female who is pregnant or can become pregnant or if I think, for ANY REASON, that my sexual partner may be pregnant. Female partners of male patients taking lenalidomide should be advised to call their own physician immediately if they get pregnant.

_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are able to have children.

_____: I agree any unused drug supply will be returned as instructed through the Revlimid REMS® Program.

_____: I know that I cannot donate blood, sperm or semen while taking lenalidomide and for 28 days after stopping lenalidomide.

FOR FEMALES THAT ARE ***NOT*** ABLE TO BECOME PREGNANT

Please read thoroughly and initial each space provided if you understand each statement.

_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.

_____: I certify that I am not now pregnant, nor am I of child bearing potential as I have been in a natural menopause for at least 24 months (been through the change in life without even 1 menstrual period for the past 24 months); or I had my uterus removed (hysterectomy) or had both my ovaries removed (bilateral oophorectomy).

_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children.

_____: I agree any unused drug supply will be returned as instructed through the Revlimid REMS® Program.

_____: I know that I cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.

All Patients Taking Lenalidomide

You will be counseled at least every 28 days either by counselors at the site or through the Revlimid REMS® program during lenalidomide treatment and again one last time when you stop taking lenalidomide about not sharing lenalidomide (and other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies" with each new supply of lenalidomide as a reminder of these safety issues.

Other Information:

There may be some unknown or unanticipated discomforts or risks associated with this treatment in addition to those specified above, but every precaution will be taken to assure your personal safety and to minimize discomforts.

Throughout the study, the researchers will tell you of new information that might affect your decision to remain in the study.

If you wish to discuss the information above or any other discomforts you may experience, you may ask questions now or call your doctor _____, the Principal Investigator or contact person listed on the front page of this form.

9a. What are the possible benefits to you for taking part in this study?

Although this study cannot be guaranteed to be of benefit to you, it is hoped that your taking part may lead to the improvement or "temporary" disappearance of your myeloma and prolongation of your life. However, no benefit is guaranteed.

9b. What are the possible benefits to others?

A possible advantage of this study is that benefit to others may result from the knowledge gained from your participation in this research study.

10. If you choose to take part in this study, will it cost you anything?

You are responsible for the costs of treatment for your disease on this protocol. Your insurance provider may not cover all or part of these costs. You are not required to pay for tests or research samples that are being performed or collected only for research purposes. Two drugs from consolidation treatment (lenalidomide and bortezomib) and maintenance (3 years of lenalidomide) are being provided by the manufacturers free of charge. If you have concerns or questions regarding coverage or potential charges, you should contact (contact person's name) at (###) ###-####, or the Principal Investigator of the study, to review the situation.

11. Will you receive payment for taking part in this research study?

No, you will not receive payment for taking part in this research study. Your participation in this study may result in discoveries or products. The discoveries and products may have commercial value, and if there is commercial value, you will not receive any compensation from the discoveries or products.

12. What if you are injured because of the study?

It is important that you tell your study doctor or study staff if you feel that you have been hurt or injured because of taking part in this study. You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. This study will not pay for medical treatment. In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form. If you have any questions about injuries, you may call [insert name] at (###) ###-####.

13. What other options or treatments are available if you do not want to be in this study?

Participation in this study is entirely voluntary. You are free to refuse to be in the study, and your refusal will not affect current or future health care you receive at this institution. You and your doctor will discuss any other treatment options available to you.

Current therapies for multiple myeloma include:

- Chemotherapy using single 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 and other possible treatment approaches with you.

13a. How can you withdraw from this research study?

If you agree to be in this study, you are free to change your mind. At any time you may withdraw your consent to be in this study and for us to use your data. If you withdraw from the study, you will continue to have access to health care at [participating clinical facility]. If you decide to withdraw, we ask that you tell the [Principal Investigator] in writing; his/her mailing address is on the first page of this form. If you do withdraw your consent, there will be no penalty and you will not lose any benefits to which you are otherwise entitled.

Due to the nature of your illness and the study treatments, it is important to continue to receive medical follow-up even if you withdraw from the research study. If you have any questions about your rights as a study subject, you may call the Institutional Review Board (IRB) office at (###) ###-####.

13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, we ask that you agree that we can continue using all information about you that has already been collected as part of the study prior to your withdrawal, and to continue to allow your doctor to tell us about your progress until 12 months after your transplant. You may, of course, say no.

13c. Can the Principal Investigator withdraw you from this research study?

You can be taken off the study (with or without your consent) for any of the following reasons:

- You do not qualify to be in the study because you do not meet the study requirements.
- You need a medical treatment not allowed in this study.
- The investigator decides that continuing in the study would be harmful to you.
- The study treatments have a bad effect on you.
- You become pregnant as the study treatment could be harmful to the fetus.
- You are unable to keep appointments or take study drugs as directed.
- Other study-specific reasons; for example, if the study treatment you are taking has been found to be unsafe.
- The study is cancelled by the Food and Drug Administration (FDA) or the National Institutes of Health (NIH).
- Your myeloma returns.

14. How will your privacy and the confidentiality of your research records be protected?

Study records that have your name will be kept private as required by law. You will not be identified by name in the central study records. Your records will be given a unique code number. The key to the code will be kept in a locked file in the offices of the Coordinating Center for the study. Authorized persons from the [participating clinical facility], the hospital or clinic (if any) involved in this research, and the Institutional Review Board have the legal right to review your research records and will protect their confidentiality to the extent permitted by law. This research study is sponsored by and conducted with funds from the National Institutes of Health; therefore, the sponsor, the sponsor's agent, the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), the investigators conducting this study, Southwest Oncology Group, the Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials, the NCI-sponsored Cancer Cooperative Groups that enroll patients on this trial through the CTSU, and the FDA also have the legal right to review your research records. Otherwise, your research records will not be shown to anyone without your consent unless required by law or a court order.

If the results of this research are published or presented at scientific meetings, your name will not be disclosed.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

15. Expiration date for retention of records

The study results will stay in your research record at [insert Institution] for at least six years or until after the study is completed, whichever is longer. At that time either the research information not already in your medical record will be destroyed or your name and other identifying information will be removed from such study results. Research information in your medical record will be kept indefinitely.

16. How will the researcher(s) benefit from your being in this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator may benefit if the results of this study are presented at scientific meetings or in scientific journals. In addition, the sponsor is providing funds to the Principal Investigator to facilitate the conduct of this study.

17. HIPAA[2] authorization to use and disclose individual health information for research purposes

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study entitled *A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma.*

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment), physical examination findings, and laboratory test results obtained at the time of work-up and after transplantation (e.g., bone marrow tests, blood tests, biopsy results).

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from (*list hospitals, clinics or providers from which health care information can be requested*).

_____

_____

_____

d. Parties Who May Receive or Use My Individual Health Information: The individual health information disclosed by parties listed in item "c." above and information disclosed by me during the course of the research may be received and used by the following parties:

2 HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information.

- Principal Investigator and the researcher's staff
- Dr. Amrita Krishnan, Study Chairperson and staff/laboratories at City of Hope National Medical Center
- Dr. George Somlo, Study Chairperson and staff/laboratories at City of Hope National Medical Center
- Dr. Edward Stadtmauer, Study Chairperson and staff/laboratories at University of Pennsylvania Cancer Center.
- National Heart, Lung, and Blood Institute (NHLBI) and National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN), data and coordinating center, including the Center for International Blood and Marrow Transplant Research (CIBMTR), The National Marrow Donor Program (NMDP), and The EMMES Corporation.
- The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.
- The NCI-sponsored Cancer Cooperative Groups that enroll patients on this trial through the CTSU
- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments
- Celgene (the manufacturer of lenalidomide)
- Biologics, Inc (the distributor of lenalidomide)
- Millennium Pharmaceutics (the manufacturer of Bortezomib)

e. Right to Refuse to sign this Authorization: I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research-related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

f. Right to Revoke: I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

g. Potential for Re-disclosure: My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected. Examples include potential disclosures for law enforcement purposes,

mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

h. This authorization does not have an expiration date.

18. Further Information

If you have further questions concerning this project at any time, you are free to ask them of Dr. _____, who will be available to answer them. His/her telephone number is located on the first page of the consent.

19. Consent Instructions

<u>To voluntarily become a participant in this research study I must confirm the following and sign below.</u>

* I have read all of the information in the Informed Consent and I have had time to think about it.
* All of my questions have been answered to my satisfaction. If I did not understand any of the words or parts of this study, I asked the study doctor or the research staff to explain what I did not understand.
* I voluntarily agree to be part of this research study and to follow the study procedures as directed. I agree to keep the research staff informed of my current contact information.
* I have been informed that I may discontinue my participation in this study at any time.
* Signing this consent form is not a waiver of my legal rights.
* I have received a signed copy of this Informed Consent to keep for my reference.

 Patient Initials _____

Subject Name (please print)

Subject Signature or Legal Representative (relationship) Date & Time

Name of Individual Conducting Informed Consent Discussion
(please print)

Signature of Individual Conducting Informed Consent Discussion Date

Signature of Witness (where Applicable) Date

I have fully explained the research study to the subject and answered all of the subject's questions.

Name of Principal Investigator or Authorized Representative
(please print)

Signature of Principal Investigator or Authorized Representative Date