INFORMED CONSENT DOCUMENT

Project Title: **Single Autologous Transplant followed by Consolidation and Maintenance for Participants ≥ 65 Years of Age Diagnosed with Multiple Myeloma or a Related Plasma Cell Malignancy.**

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Research Team Contact: Meghan Chandler, RN
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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have been diagnosed with multiple myeloma or POEMS **(**Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, and Skin changes, which is a syndrome in which patients have a plasma cell disease resembling multiple myeloma, and various organ changes).

The purpose of this research study is to find out whether relapse or disease progression will be delayed when an autologous stem cell transplant (a transplant using your own stem cells) is combined with consolidation and maintenance treatment after transplant, and how safely this treatment can be given in patients with myeloma who are 65 years of age or older.

All of the drugs that will be used are commercially available, are FDA approved for one or more cancers, and have been used in the treatment of multiple myeloma and/or other cancers. However, the drugs Doxorubicin, Etoposide, and Cisplatin are not FDA approved specifically for the treatment of multiple myeloma.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 41 people will take part in this study conducted by investigators at the University of Iowa. This study will only be conducted at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement in the study treatment portion of this protocol will take approximately 2.3-3 years if you complete the entire study treatment schedule. Whether you stop early or complete study treatment, we will continue to follow you 1-3 times per year after treatment is done until one or more of the following occurs:

- your disease progresses
- you choose to stop participating in the study
- you become pregnant during the course of study treatment if you are a female of childbearing age (although we will follow you through the course of your pregnancy)
- your treating physician or the Principal Investigator believes it is in your best interest to stop your participation in the study
- you do not follow instructions for participation in the study

During each follow-up visit, you will see your study physician for approximately one hour, and the research coordinator for approximately 15 minutes.

During the first phase of study treatment, which may be completed within 3-12 months, you will have 4-5 study visits at the following time points:

- before the induction phase
- before transplant
- before consolidation treatment if you receive this study treatment step
- before proceeding to the first year of maintenance therapy

Each of these study visits will also require a time commitment of approximately one hour with your study physician, and approximately 15 minutes with the research coordinator.

WHAT WILL HAPPEN DURING THIS STUDY?

Participation in this study will involve multiple phases.

Before the study treatment begins, you will have screening tests and procedures for your disease that are part of your regular cancer care. Based on these results, the study team will be able to determine if you are a good candidate to continue in this study.

Although we try to give as much of your research treatment in an outpatient setting, it is highly likely that you may experience one or more hospitalizations during the course of this study, either because of the disease itself, because of complications of the study treatment, or because the study treatment cannot be given safely to you as an outpatient. Thus, some of these study treatments may need to be given while you are hospitalized. Only the study treatments prior to the maintenance phase must be given through the University of Iowa Holden Comprehensive Cancer Center.

Induction Phase: If you are eligible to receive study treatment, you will begin the induction phase. During this phase, you will receive chemotherapy, and when your blood counts recover, you will have your stem cells collected.

The following tests may be performed if you do not start induction treatment within 2 weeks of study enrollment. If you do start study treatment within 2 weeks of study enrollment, we will use the pre-study test and procedure results.

- Blood samples (approximately 9-11 tablespoons) will be done for routine blood count, chemical analysis, to measure specific blood markers related to your disease, and to see how well your organs are functioning. If you are a woman of child-bearing age, we will also perform a pregnancy test.
- You will also have a bone marrow aspirate and biopsy done.
- The doctor may also order a PET (positron emission tomography) or MRI (magnetic resonance imaging) scan to assess the full extent of your disease.
- You will have a physical examination.

You will receive chemotherapy drugs that are called DPACE (dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide). We will provide you with a study treatment calendar. The chemotherapy drugs will be administered according to the following schedule:

Dexamethasone 20 mg oral (by mouth) on days 1-4 and 8-11.

Cisplatin 10 mg/m^2/day on days 1-4 Continuous Infusion (CI).

Doxorubicin 10 mg/m^2/day on days 1-4 CI.

Cyclophosphamide 400 mg/m^2/day or 600 mg/m^2 on days 1-4 CI.

Etoposide 40 mg/m^2/day on days 1-4 CI.

An assessment of any side effects or adverse reactions will be made, and we will also review medications with you to ensure that you have taken the oral drugs according to the study schedule. We will give you medication and side effect diaries to assist the study team with these assessments. We will ask you to complete these diaries on a daily basis and bring them back to the study team at your next study visit or you may also fax or e-mail these diaries using the contact information provided to you on those forms.

Once you recover your blood counts after chemotherapy (usually between days 12 and 17), you will have your stem cell collection. The goal of this stem cell collection is to obtain enough cells for a transplant in the near future and to have additional stem cells in store in case you need a stem cell boost, or you need another stem cell transplant in the future because the myeloma has recurred. The more stem cells we collect, the safer your transplant will be. If the amount of stem cells collected is inadequate, you may need another stem cell collection.

A stem cell boost refers to an additional infusion of your own stem cells after transplant (but without additional chemotherapy) because your blood counts have not recovered (graft failure) or are slower to recover (graft delay) after transplant than expected, which leaves a patient vulnerable to infections and an extended need for blood transfusions. This delay or lack of recovery in your blood counts increases your risk of serious complications after transplant.

Although unlikely, it is possible that the first stem cell collection may contain too many myeloma cells, and using these contaminated cells with your transplant is riskier. Therefore, if this would happen, you will undergo an additional round of chemotherapy (VDT-PACE) prior to any additional stem cell collections. The administration schedule for this round of chemotherapy called VDT-PACE is as follows:

Dexamethasone 20 mg oral on days 1-4 and days 8-11

Thalidomide 100mg oral on days 1-11

Bortezomib 1mg/m^2 IV Push (administered quickly) on days 1, 4, 8, 11

Cisplatin 10 mg/m^2 on days 1-4 CI

Doxorubicin 10mg/m^2 on days 1-4 CI

Cyclophosphamide 400 mg/m^2 on days 1-4 CI

Etoposide 40 mg/m^2 on days 1-4 CI

After the stem cell collection, you will continue to receive Dexamethasone for 4 days in a row every 14 days.

Transplant: Anywhere between 4 weeks and 6 months after the first day of DPACE), you will have your transplant. Before the transplant takes place, you will have the following tests and procedures done as part of your regular care.

- Blood samples (approximately 9-11 tablespoons) will be done for routine blood count, chemical analysis, to measure specific blood markers related to your disease, and to see how well your organs are functioning. A pregnancy test will be added if you are a woman of child bearing potential.
- You will also have a bone marrow aspirate and biopsy done.
- You may also have an MRI (magnetic resonance imaging) scan and/or PET (positron emission tomography) scan. These scans will be used to assess your response to the induction chemotherapy, but may also be done to see if there are any signs of infection present.
- You will have a physical examination.
- An assessment will be made of any side effects or adverse reactions that you have had or are having, and we will also review medications with you to ensure that you have taken the oral drugs according to the study schedule. We will give you medication and side effect diaries to assist the study team with these assessments. We will ask you to complete these diaries on a daily basis and bring them back to the study team at your next study visit or you may also fax or e-mail these diaries using the information provided to you on those forms.

As part of the transplant, you will be receiving chemotherapy drugs called bortezomib, thalidomide, dexamethasone, and melphalan. The day after your second dose of melphalan, you will have the

transplant, which means that part of your previously collected stem cells will be given back to you. The day of your transplant is considered day 0. We will provide you with a treatment calendar. The chemotherapy drugs will be administered according to the following schedule:

Dexamethasone 20 mg oral on days -4 to -1 and +2 to +5.

Bortezomib 1mg/m^2 IV Push (administered quickly) on days -4, -1, +2, and +5.

Thalidomide 100mg/day oral on days -4 to +5.

Melphalan will be given at a dose of 100 mg/m^2 on days -4 and -1 (Patients > 70 years of age or with a creatinine > 2.0 mg/dl will receive a reduced dose of Melphalan of 70 mg/m^2 on days -4 and -1).

Peripheral blood stem cell infusion will be given intravenously on day 0, at least 18 hours after the second dose of melphalan.

Once you have recovered from most of the side effects of the transplant, you will restart thalidomide daily and dexamethasone for four days every 21 days.

Consolidation Phase: Approximately 4 weeks to 4 months after transplant, you will have the following tests and procedures done as part of your regular care.

- Blood samples (approximately 9-11 tablespoons) will be done for routine blood count, chemical analysis, to measure specific blood markers related to your disease, and see how well your organs are functioning. A pregnancy test will be added if you are a woman of child bearing potential.
- You will also have a bone marrow aspirate and biopsy done.
- You may also have an MRI (magnetic resonance imaging) scan and/or PET (positron emission tomography) scan. These scans will be used to assess your response to transplant, but also to see if there are any signs of infection present.
- You will have a physical examination.
- An assessment will be made of any side effects or adverse reactions that you have had or are having, and we will also review medications with you to ensure that you have taken the oral drugs according to the study schedule. We will give you medication and side effect diaries to assist the study team with these assessments. We will ask you to complete these diaries on a daily basis and bring them back to the study team at your next study visitor you may also fax or e-mail these diaries using the information provided to you on those forms.

As part of the consolidation phase, you may receive the chemotherapy drugs dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide. **However, most patients will not receive consolidation treatment.** If you have high-risk disease, have recovered from transplant, and had at least a partial response to induction therapy, you will receive consolidation chemo. If you receive consolidation treatment, we will provide you with a treatment calendar. The chemotherapy drugs will be administered according to the following schedule:

Dexamethasone 20 mg oral on days 1-4 and days 8-11

Thalidomide 100mg oral on days 1-11

Bortezomib 1mg/m^2 IV Push (administered quickly) on days 1, 4, 8, 11

Cisplatin 10 mg/m^2 on days 1-4 CI

Doxorubicin 10mg/m^2 on days 1-4 CI

Cyclophosphamide 400 mg/m^2 on days 1-4 CI

Etoposide 40 mg/m^2 on days 1-4 CI

Maintenance Phase Year 1 and 2: After you have completed the consolidation phase, or if you do not receive consolidation treatment, you will proceed to maintenance. During these two years, the following tests and procedures will be done as part of your regular care.

- You will have a physical examination.
- At least 3 times per year you will have certain blood tests done to measure your blood chemistry, disease markers, and organ function. Other blood tests may be done, or blood tests may be performed more frequently, if your study doctor determines that it is necessary.
- At least 3 times per year, you will also have a bone marrow aspirate and biopsy.
- MRI or PET scans will be done if clinically necessary, as determined by your study doctor.
- An assessment will be made of any side effects or adverse reactions that you have had or are having, and we will also review medications with you to ensure that you have taken the oral drugs according to the study schedule. We will give you medication and side effect diaries to assist the study team with these assessments.

After year 2 of maintenance treatment has been completed, we will continue to follow you 1-3 times per year as long as you remain on study.

Long-term follow-up

During all subsequent years, the following tests and procedures will be done as part of your regular care.

- At least once per year, you will have a physical examination.
- At least once per year, you will have blood tests done to measure your blood chemistry, disease markers, and organ function. These blood tests, or other blood tests, may be done more frequently if your study doctor thinks that they are clinically necessary.
- At least once per year, you will have a bone marrow aspirate and biopsy.
- MRI or PET scans will only be done if clinically indicated and determined as necessary by your doctor.

Quality-of-Life Questionnaires

Another optional part of this study involves the administration of quality-of-life questionnaires that the study team will provide you. These questionnaires will help the study team understand what quality-of-life is like before, during, and after this type of treatment plan when given to patients who are 65 years of age or older.

If you agree to participate in this part of the study, you will complete 2 quality-of-life questionnaires that have been given to thousands of cancer patients involved in clinical trials internationally at the following time points:

- Before you begin any study treatment but after you have signed a consent form for this study.
- Before consolidation or maintenance treatment (if consolidation is skipped) begins
- Three times per year at your clinic appointments during maintenance treatment
- Once per year thereafter for as long as you continue to be enrolled in this study, even when you are finished with study treatment.

The first questionnaire is a more generic assessment of symptoms and your overall health, while the second questionnaire is focused on more common myeloma-specific symptoms that not all cancer patients might experience. Both questionnaires should take you approximately 3-5 minutes to complete. Answers to the questionnaires are kept completely confidential. There is a small possibility that you may be distressed by some of the questions, although a lot of the questions are very similar to those that a physician might ask you in order to understand how you are doing.

If you agree at this time to complete these questionnaires but decide in the future that you would like to withdraw your participation from this part of the study, please contact Meghan Chandler, RN by phone (319-467-5836) or via e-mail at meghan-chandler@uiowa.edu

Please place your initials in the blank next to Yes or No for each of the questions below:

I agree to complete the 2 quality-of-life questionnaires throughout my involvement in this study.

_____ Yes _____ No _____ Initials

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Cancer treatments have side effects that can range from mild to severe. With your cancer treatment you are likely to experience a number of side effects, and some of these may be serious. These may include additional hospitalizations and even death.

It is expected that 5 to 10% of patients will die of complications of the study treatment. Deaths with this type of treatment are usually due to infections that develop when the immune system, due to

the high doses of chemotherapy, is less able to fight off infection successfully. It is therefore extremely important that you follow all of the instructions related to preventing infections closely.

Based on research studies at the University of Arkansas using similar treatment, 12% of patients over the age of 65 died from this type of treatment. Although we do not expect this to be the case in this study since this study treatment is not as intensive and includes only a single transplant, it is possible that we may also see a similarly higher rate (12-15%) of study-related deaths, since most of the deaths were observed with the first transplant or during the consolidation/maintenance therapy. However, although the risk of this treatment is higher, we hope that this treatment will result in better and longer control of your cancer (48 months versus an average of 24-36 months with non-transplant chemo) and a good quality-of-life. **Please consider the possible benefits and risks very carefully before deciding to participate in this study.**

Common side effects of many chemotherapy drugs include: nausea, vomiting, hair loss, upset stomach, and low blood counts. Low blood counts put a patient at risk of infection, bleeding, and anemia. Sometimes low blood counts may require transfusions to bring the counts back up.

Rarely, a patient may have an allergic reaction to chemotherapy, or may have evidence of a serious condition called tumor lysis syndrome, which refers to major changes in various laboratory values as a result of dying tumor cells releasing their contents into the blood stream. This could result in damage to various organs, including the heart, kidneys, and liver. Sometimes patients also have complications from the central lines used for giving chemotherapy or collecting stem cells. These complications can include developing a blood clot at the site of the line, and line-related infections.

Another potential side effect of a transplant in which your own stem cells are used is a syndrome called engraftment syndrome. In a paper published by University of Wisconsin researchers, engraftment syndrome was referred to as autologous graft-versus-host disease. While your blood counts are recovering, the symptoms of engraftment syndrome may include fever, a skin rash, and fluid build-up in the lungs. These symptoms are due to the interactions between the body's cells and small proteins that are important in cell signaling. In its less severe form, engraftment syndrome occurs in approximately 9% of patients. In extremely rare cases, the fluid build-up in the lungs may lead to lung failure or other organ failure, but this occurs in less than 2% of patients. Steroids are used to treat the symptoms of engraftment syndrome, and this usually resolves the symptoms.

RISKS/SIDE EFFECTS ASSOCIATED WITH THE INDIVIDUAL CHEMOTHERAPIES

Bortezomib

Common (equal to or greater than **30%):** fatigue, generalized weakness, peripheral neuropathy (numbness and/or tingling in the hands or feet, which can be painful), nausea and/or vomiting, diarrhea, loss of appetite, constipation, low platelet counts, fever, low red blood cell counts.

Less Common (10-29%): headache, difficulty sleeping, joint pain, swelling of the face, hands, feet, or legs, low white blood cell counts, shortness of breath, dizziness, rash, dehydration, respiratory tract infections, cough, bone pain, anxiety, muscle cramps, heartburn, abdominal pain, low blood pressure, itching, blurring of vision, electrolyte abnormalities (low potassium, low magnesium, etc).

Rare but Serious (less than **10%):** serious abnormal heart rhythms, congestive heart failure, lung disorders, liver failure, Reversible posterior leukoencephalopathy syndrome (a reversible condition of the brain that results in seizures, high blood pressure, headaches, tiredness, confusion, blindness, and other vision problems).

Carfilzomib

Common (equal to or greater than **30%):** low platelet counts, fatigue, low red blood cell counts, nausea, shortness of breath, diarrhea, and fever.

Less common (10-29%): pneumonia, low white blood cell counts, lack of appetite, pain, high blood sugar, higher than normal blood levels of calcium, phosphorus, and sodium, mild decrease in kidney function, peripheral neuropathy (numbness and tingling in your hands and feet).

Rare but serious (less than **10%):** decrease in heart function ranging from mild to severe, pulmonary hypertension (an increase of blood pressure in the lung arteries), infusion reactions ranging from mild to severe, tumor lysis syndrome (changes in laboratory values as a result of dying tumor cells releasing their contents into the blood stream. This could result in damage to various organs, including the heart, kidneys, and liver), liver failure, infection requiring hospitalization, shingles.

Cisplatin

Common (equal to or greater than **30%):** low white blood cell counts, low red blood cell counts, low platelet counts, electrolyte abnormalities (i.e. low magnesium, low potassium, etc), temporary kidney dysfunction.

Less Common (10-29%): peripheral neuropathy (numbness and/or tingling in the hands or feet) which may be irreversible, ringing in the ears, loss of appetite, metallic taste in the mouth, temporary increases in liver enzymes, hair loss, infertility.

Rare but Serious (less than **10%):** loss of vision, swelling of the eye(s), hearing problems, heart attack, stroke, inflammation of arteries in the brain, leaking of plasma from blood vessels, seizures, puffy face, fast heartbeat, electrolyte imbalances, hormone imbalances, changes in the brain's white matter that do not have any known clinical or neurologic consequences.

Cyclophosphamide

Common (equal to or greater than **30%):** low white blood cell count, low red blood cell counts, low platelet counts, temporary hair loss, nausea and vomiting, loss of appetite, infertility, discoloration/darkening of the skin and nails.

Less Common (10-29%): diarrhea, mouth sores, bladder problems, including bladder irritation and bleeding, kidney damage, hormone imbalances, sweating, temporary redness of the face and neck, head pain, increase in uric acid that could lead to gout or kidney stones.

Rare but Serious (less than **10%):** painful, red, or swollen mouth, hepatitis (inflammation of the liver), trouble breathing, allergic reaction, development of a blood cancer.

Dexamethasone

Common (equal to or greater than **30%):** increased appetite, irritability, insomnia (difficulty sleeping), swelling in the ankles and/or feet, heartburn, muscle weakness, impaired wound healing, increases in blood sugar levels.

Less Common (10-29%): headaches, dizziness, mood swings, cataracts, bone thinning, intestinal bleed, osteoporosis, diabetes, Cushing's Syndrome (hormone disorder that results in too much cortisol), irregular menstrual periods.

Rare but Serious (less than **10%):** depression that may lead to suicidal tendencies, mania (extreme sense of wellbeing), increased pressure in the eye, high blood pressure, severe muscle weakness, slow heartbeat, abnormal heart rhythm, blood clots, hallucinations, abnormal liver enzymes, confusion.

Doxorubicin

Common (equal to or greater than **30%):** Low white blood cell count, low platelet count, low red blood cell count, nausea and/or vomiting, diarrhea, heart rhythm disturbances with no clinical consequences, fever and risk of infection, temporary hair loss, sores in the mouth, weakness, loss of appetite.

Less Common (10-29%): watery eyes, red-orange tint to the urine, darkening of the skin or nail beds, infertility.

Rare but Serious (less than**10%):** congestive heart failure (with higher doses), inflammation of the heart muscle, heart rhythm abnormalities, ulceration of the colon, swelling/rash or other abnormality at the IV site, hypersensitivity/allergic reaction, kidney dysfunction, redness or swelling of the eye, decreased vision, and the development of another cancer.

Etoposide

Common (equal to or greater than **30%):** low white blood cell counts, low platelet counts, low red blood cell counts, hair loss, menopause, infertility, nausea and vomiting, low blood pressure.
Less Common (10-29%): mouth sores, diarrhea, loss of appetite, metallic taste in mouth, peripheral neuropathy (numbness and tingling in the hands or feet), low blood pressure, constipation.

Rare but Serious (less than **10%):** allergic reactions, development of a blood cancer.

Lenalidomide

Common (equal to or greater than **30%):** back pain, low platelet counts, low white blood cell counts, diarrhea, itching of the skin, rash, mild stomach pain, stuffy or runny nose, fatigue.

Less Common (10-29%): headache, blood clots, nausea and/or vomiting, constipation, low red blood

cell counts, abdominal pain, dry mouth or skin, night sweats, edema (fluid retention in the feet or ankles), respiratory tract infections, pneumonia, shortness of breath, nosebleed, joint pain, back pain, muscle cramping, muscle weakness, dizziness, peripheral neuropathy (numbness and/or tingling in your hands or feet), urinary tract infection, low blood potassium levels, loss of appetite, trouble sleeping.

Rare but Serious (less than **10%):** splenic infarction (death of spleen tissue due to a blockage of blood flow), myelodysplasia (condition in which the bone marrow fails to produce adequate red blood cells or platelets), intestinal bleeding, intestinal perforation (a hole or tear develops in the intestinal wall), intestinal inflammation or infections, inflammation of the pancreas, severe skin reactions, including the development of a skin disease called Stevens-Johnson syndrome, which may be fatal, bone fractures, memory impairment, stroke, migraines, kidney dysfunction or failure, kidney infections, diabetes, low blood sugar levels, inflammation of the gallbladder, inflammation of the liver, abnormal thyroid function, high blood pressure, depression, delusions, congestive heart failure, abnormal and serious heart rhythm abnormalities, blood clot in the lungs, and the development of another cancer.

Melphalan

Common (equal to or greater than **30%):** low white blood cell counts, low red blood cell counts, low platelet counts, nausea and/or vomiting.

Less Common (10-29%): allergic reaction, mouth sores, diarrhea, infertility, hair loss, kidney dysfunction, abnormal heart rhythms that may or may not be clinically significant.

Rare but Serious (less than **10%):** anaphylaxis (serious allergic reaction that could be life-threatening), jaundice (yellowing of the skin or eyes), problems breathing, liver damage, development of another cancer.

Pomalidomide

Common (equal to or greater than **30%):** fatigue, weakness, low white blood cell counts, low red blood cell counts, constipation, nausea, diarrhea, shortness of breath, lung infections, back pain, and fever.
Less common (10-29%): muscle weakness, pneumonia, bone pain, cough, nose bleed, decrease in appetite, higher than normal blood sugar levels, higher than normal calcium levels, low potassium levels, low sodium levels, rash, itchy skin, dizziness, headache, neuropathy (numbness and tingling in your hands or feet), confusion, anxiety, decrease in kidney function.

Rare but Serious (less than **10%):** Chills, pain, urinary tract infection, lower than normal calcium levels, excessive sweating, night sweats, dry skin, tremor, insomnia.

Thalidomide

Common (equal to or greater than **30%):** fatigue and some form of neuropathy (numbness and/or tingling in the hands or feet).

Less Common (10-29%): dizziness, peripheral neuropathy interfering with the daily activities of life, low red blood cell counts, low white blood cell counts, fever, sweating, acne, nausea, constipation or

much less likely diarrhea, blood in the urine, increases in liver enzymes, mood changes.

Rare but Serious (less than **10%):** migraines, confusion, seizures, fainting, enlarged spleen, infection, urinary incontinence, tremor, diabetes, increased blood cholesterol levels, high and low blood pressure, congestive heart failure, a slow heart rate or other serious abnormal heart rhythms, blood clots, blood clots in the lungs, heart attack, stroke, liver function abnormalities, enlarged liver, jaundice associated with gallbladder disease, liver failure, obstruction of the bile duct, pneumonia, thyroid dysfunction, deafness, ringing in the ears, suicide attempts, psychosis, kidney failure, and the development of another cancer.

OTHER RISKS ASSOCIATED WITH STUDY TREATMENT

Transplant

1. DSMO: when your stem cells are collected, a preservative called DSMO (dimethylsulfoxide) is added to them before they are frozen, and the side effects associated with this preservative are: facial flushing, tickling sensation in the throat, strong taste in the mouth, strong odor, diarrhea, abnormal heart rhythms, nausea and/or vomiting, reddish urine, and rarely, abdominal pain, seizures, and kidney failure. To minimize these side effects, you will be premedicated before the infusion, and you will receive a sterile saline infusion after the transplant to help flush this preservative out of your body. Furthermore, your transplant will be split over two days if the amount of DMSO is above certain levels.

2. Allergic reaction/anaphylaxis: you may experience an allergic reaction (chills, fever, and hives) to the proteins or other parts of the stem cell infusion. Anaphylaxis is a severe and sometimes life-threatening whole-body allergic reaction. You will be treated immediately if any signs of allergy or anaphylaxis arise.

3. High and low blood pressure: Blood pressure fluctuations can occur. The stem cell infusion may have to be slowed or temporarily interrupted to allow your blood pressure to normalize.

3. Pulmonary Micro-Embolism (small clots that have traveled to the lungs): Clumps of cell matter may have formed after thawing your stem cells, and these clumps could result in micro-emboli in the lungs, which could be very serious. Symptoms include chest pain, shortness of breath, or coughing. Slowing of the infusion and administration of oxygen may alleviate mild shortness of breath during infusion.

4. Fluid build-up in the lungs: Rarely, patients may experience fluid build-up in the lungs, which is generally associated with a higher volume infusion. Slowing the stem cell infusion and supplemental oxygen may be necessary to treat symptoms.

5. It is possible that your infused stem cells may be slow to engraft (regrow your bone marrow). This may be due to infection, medications, damage to the stem cell product during freezing, or a lower number of stem cells infused. This is known as graft delay. If this occurs, your physicians may need to infuse additional stem cells to help your bone marrow recover faster. The risks of this additional infusion are the same as the risks of transplant (not including the chemotherapy) outlined in this section.

6. Graft failure, in which bone marrow function fails to return, is extremely unusual when a patient's

own stem cells are the source of the stem cell infusion. Graft failure occurs in less than 1% of autologous (using one's own stem cells) transplants.

Post-transplant Transfusions

After the transplant, you will have low levels of red blood cells, white blood cells, and platelets, and you may need transfusions. There are risks with blood transfusions, which include transfusion reaction, infections, and fluid overload (too much fluid). The most frequent signs of transfusion reaction are fever, chills, itching, and hives. Most blood transfusions go well and without complication, and only very rarely do serious problems develop.

Growth Factors

Before your stem cell collection and after the transplant, you will receive growth factors called filgrastim or pegfilgrastim, which are drugs that will prompt your bone marrow to produce more white blood cells. The risks of receiving filgrastim or pegfilgrastim include fevers and bone pain, which may be severe and require pain medication. Other risks are more serious but rare. They include a very high concentration of white blood cells which can cause strokes and heart attacks. However, thousands of patients have received filgrastim and there is only one report of a patient with a heart attack.

Women Capable of Becoming Pregnant

If you are a woman who is capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your fetus, or risks to your fetus that we did not anticipate, associated with being in the study. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. If you believe or know you have become pregnant while participating in this research study, please contact Meghan Chandler at 319-467-5836 as soon as possible.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study.

We hope that, in the future, other people might benefit from this study from knowledge gained toward establishing a treatment plan for patients who are only able to receive a single autologous bone marrow transplant that delays disease progression or relapse longer than other currently used treatment options but can also be administered safely in patients age 65 and older.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Options available as an alternative to taking part in this study include:

- Different non-transplant combinations of chemotherapy drugs commonly used in the treatment of multiple myeloma.

- Stem cell transplant off study (either as a single or double autologous transplant).
- Participation in another research study
- No treatment

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have costs for being in this research study. You and/or your insurance company will need to pay for all of the costs of treating your cancer while in this study. Some insurance plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Financial coordinators are available to assist you with insurance coverage questions or issues.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- the U.S. Food and Drug Administration
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will only conduct study discussions, including the informed

consent discussion, in a private area. Hard copies of the study data will only contain de-identified information. Research charts containing identifying information will be kept in a locked area and will only be accessible to designated study team members or those parties outlined in the above paragraph. Electronic study data will be username and password-protected and only accessible to study team members or those parties outlined in the above paragraph. Optional blood and/or tissue samples obtained during the course of this study will only be labeled with the date, your initials, and your unique study identification number. Only the research coordinator(s) will know who donated each sample. The lab team will not have access to any of your identifying information. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

If any information from this study is published in medical journals, the published results will not identify you by name or reveal any other identifiers that may make it possible for someone to link you to this study.

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

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires the University of Iowa Hospitals & Clinics to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once the University of Iowa Hospitals & Clinics has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff. You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes the University of Iowa Hospitals & Clinics to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be

given access to your health care records by contacting your University of Iowa health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Dr. Yogesh Jethava, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, 5980 JPP, Iowa City, IA 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we may ask you to come in for a final study visit in order to ensure that we have complete safety and study information up to the point of your decision to withdraw from the study. We may also ask you to complete some lab tests if you have any side effects that still need resolution.

Will I Receive New Information About the Study while Participating?

Sometimes during the course of a research study, new information becomes available about the drugs or combinations of drugs that are part of the study design. If this happens, a study doctor will talk to you about it promptly and discuss whether you will want to continue in a study.

If you decide to withdraw at that time, your research doctor will make arrangements for your medical care to continue. Also, on receiving new information, your research doctor might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons for doing so and arrange for your medical care to continue.

If you decide to continue in the study, you will be asked to sign an updated consent form that contains the new information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the study doctors have the right to withdraw you from the study for any of the following reasons:

- Progression/relapse of disease
- Occurrence of an unacceptable side event
- Non-compliance with study requirements

- Administrative reasons
- Failure to return for follow-up
- Changes in your condition that make further study treatment unacceptable in the judgment of the study doctor(s)

If you are removed from the study, this will be clearly communicated to you during a clinic visit and noted in your research record or in a letter if you decide not to return to the University of Iowa for further care.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: **Yogesh Jethava (319-384-9067)**. If you experience a research-related injury, please contact: **Yogesh Jethava (319-384-9067)** during business hours**.** Outside of business hours, please call **319-356-1616,** and ask the hospital operator for the bone marrow transplant physician on call.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://research.uiowa.edu/hso. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

Do not sign this form if today's date is on or after the expiration date in the stamp at the top of this form.

_____ _____

(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)