NCT03398200

**INFORMED CONSENT FORM**

**A Randomized Phase II Study Evaluating the Efficacy of Hyperbaric Oxygen in Improving Blood Count Recovery in Autologous Hematopoietic Stem/Progenitor Cell Transplantation for Multiple Myeloma**

**Principal Investigator:** Omar Aljitawi, MD

**This consent form describes a research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully.**

The study staff will explain this study to you. Please ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about and discuss with family or friends.

- Being in this study is voluntary – it is your choice.
- If you join this study, you can change your mind and stop at any time.
- If you choose not to take part, your routine medical care will not be changed in any way.
- There are risks of participating and you should understand what these mean to you.

## INTRODUCTION

You are being asked to join a research study. You are being asked to take part in this study because you have multiple myeloma, a cancer of the bone marrow, and you have already agreed to receive an autologous hematopoietic stem/progenitor cell (Auto-HSPC) transplantation. This study involves the use of hyperbaric oxygen through a device called a hyperbaric oxygen (HBO) chamber.

You do not have to participate in this research study. Participating in research is different from getting standard medical care. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at the University of Rochester Medical Center (URMC).

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to, before deciding about this research.

You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating.

This research study will take place at the University of Rochester Medical Center (URMC), University of Kansas Cancer Center, and the University of Kentucky-Markey Cancer Center. At the University of Rochester Medical Center, with Dr. Omar Aljitawi as the researcher, approximately 80 subjects are expected to participate.

**BACKGROUND**

The Auto-HSPC transplantation is a type of HSPC transplant used to treat multiple myeloma. Auto-HSPC transplantation is a standard of care procedure in multiple myeloma and is associated with improved myeloma patient survival and their quality of life.

The Auto-HSPC transplant is also associated with complications related to chemotherapy, the preparative regimen chemotherapy given just prior to Auto-HSPC; these include inflammation of the linings of the mouth, or mucositis and lower white blood cell count, or neutropenia, with an increased risk of infections. These complications result in pain, antibiotic use, potential prolongation in hospitalization duration, and rarely death. Recovery from neutropenia is linked to recovery from these complications.

This research study is aimed at investigating the use of hyperbaric oxygen (HBO) therapy prior to the Auto-HSPC transplant to find out if it will shorten the period of neutropenia post-transplant. Recovery from neutropenia requires the HSPC to travel to the bone marrow to lodge, a process called homing, and then repopulate the bone marrow and produce mature blood cells, a process called engraftment. HBO therapy involves breathing 100% pure oxygen while in a sealed chamber that has been pressurized at 2 ½ times the normal atmospheric pressure. HBO therapy works through suppression of a hormone called erythropoietin or EPO.

EPO tells stem cells in the bone marrow to make more red blood cells. This hormone (called EPO) is increased when blood oxygen levels are low. When the EPO is increased, it might impair the bone marrow homing process of your transplant. Therefore, the researchers conducting this study hope to determine if providing 100% pure oxygen to you prior to your Auto-HSPC transplant will decrease this hormone, and in turn, improve the homing process and therefore recovery after your transplant.

The HBO chamber is currently housed at the Strong Wound Healing Center at 160 Sawgrass Drive, Rochester NY 14620. It is an approved device by the U.S. Food and Drug Administration (FDA) for the effective purposes of treating a wide variety of wounds and other conditions. The use of the hyperbaric oxygen for the purpose of this treatment study does not have FDA approval and is considered investigational. Investigational purposes are still being studied to find out what a safe dose is, what the side effects are, and whether or not the purpose is effective in the disease or condition being studied.

**PURPOSE**

By doing this study, researchers hope to learn the following:

- The effects of HBO therapy on the engraftment process and patient recovery following transplant.
- The effects of HBO therapy on hospital stay, blood and platelet transfusion needs, use of growth factors, and incidence and severity of mucositis.
- The effects of HBO on recovery of peripheral blood lymphocytes, including the natural killer

(NK) cell subset.
- The effects of HBO on multiple myeloma disease control.

**PROCEDURES**

Most of the procedures performed in this study are part of your regular cancer care (typically called "standard of care"). These procedures would be part of your cancer care whether or not you participate in the study. The standard of care procedures will all be explained to you by your study doctor. You may be asked to sign a separate consent form for the Auto-HSPC transplant.

If you are eligible and agree to participate in this study, the following standard of care procedures and procedures for research will take place:

Prior to Transplant:
You will be asked to sign this informed consent document.

If you decide to participate in this study, you will be assigned by chance (like flipping a coin) to one of two groups. Group 1 will receive the standard Auto-HSPC transplant and Group 2 will receive the HBO in addition to their standard Auto-HSPC. There is an equal chance that you will be assigned to either group.

You will receive standard treatment to prepare you for the Auto-HSPC transplant. This will include the following routine procedures and tests:

- Obtaining medical history and medications you are currently taking
- Physical exam with vital signs (this includes blood pressure, temperature, breathing, height, and weight)
- Routine clinical laboratory tests including blood (about 5 teaspoons) and urine tests.
- MUGA or Echo testing (used to assess heart function)
- Pulmonary (or lung) function tests
- Urine pregnancy test (if you are a female of childbearing potential). If you are pregnant, or currently breast feeding, you cannot participate in this study.

In addition, you will receive chemotherapy (melphalan) as part of your standard of care prior to the Auto-HSPC transplant. Additional information about this process and your standard of care treatment will be provided by the study doctor. You may be asked to sign a separate consent form.

- For HBO Subjects Only:
  You will visit the Strong Wound Healing Center for an HBO risk assessment visit prior to receiving your HBO therapy.

Day of Transplant:
On the day of your Auto-HSPC transplant, your doctor will perform a routine transplant evaluation. You will also have blood samples (approximately 1.5 teaspoons) taken for routine laboratory testing.

- For HBO Subjects Only:
  After your routine evaluation and laboratory testing is complete, an additional blood sample (approximately 1 teaspoon) will be collected for research purposes. This sample will be used to test for the hormone, EPO, and for proteins that control inflammation (called cytokines).

  You will then go to the Strong Wound Healing Center for the experimental HBO therapy. You are responsible for transporting yourself to and from this location and will be given instructions on where to go before and after HBO therapy. If you are prescribed a medication to relax you (sedative) related to HBO therapy, you will need to arrange for transportation to and from the Strong Wound Healing Center.

  You will lie in a single hyperbaric chamber where 100% oxygen will be released, pressurized at 2 ½ times the normal atmospheric pressure. The following will occur during this time:
    - For about the first 10-15 minutes in the chamber, the air pressure will be increased, and the 100% oxygen will fill the chamber.
    - During the 2 hours, there will be compression and decompression phases for 10 minutes each in which you will be breathing compressed environmental air (21% oxygen).
    - After you breathe the 100% oxygen at increased pressure for 90 minutes, the chamber will need to decompress. This takes about 10-15 minutes.

  After you receive the HBO therapy, you will be admitted to the hospital. It is recommended that you shower at the hospital using chlorhexidine (CHG) soap (which will be provided to you), but it is not required. Four additional blood samples (approximately 1 teaspoon each), for research will then be collected at the following time points to test for cytokines and EPO:
    - 6 hours after the start of HBO therapy (prior to the Auto-HSPC transplant)
    - 8, 24, and 48 hours after the start of HBO therapy.

  Following the 6 hour blood draw for research, you will receive your scheduled HSPC transplant. Within 24 hours of your HBO therapy, you will have a physical exam and your vital signs will be measured to check for any side effects that may have been caused by the HBO therapy.

After Transplant:
You will be evaluated daily until your white blood cells begin to recover. If your condition allows, you may be scheduled to be seen as an outpatient with visits scheduled 1-2 times a week, at the discretion of the study doctor. Patients who complete HBO therapy will be asked to complete a survey regarding there HBO therapy experience on day +15 post-transplant. Follow up visits will continue until 100 days post-transplant to check for side effects and up to one year for severe side effects and for response assessment.

You will have routine exams and monitoring during this time to check for symptoms related to study intervention in specific or to transplant in general. In total, about 1 1/2 teaspoons of blood will be collected for your routine laboratory tests per day after your transplant, until your white blood cells begin to recover.
Your total length of participation, including the after transplant follow-up care, will be up to

approximately 1 year. A table of study events is included at the end of this consent form.

Storage of Samples Used for Research:
Approximately 5 total teaspoons of blood will be collected for research in this study. The blood samples used for research will have all identifying information about you removed (name, date of birth, etc.). The identifying information will be replaced with a unique code. Then, they will then be sent to the Clinical Trials Office (CTO) at Wilmot Cancer Institute (WCI) laboratory for processing and storage. After all samples have been collected for this study, they will be analyzed. Samples from this study could be used by other investigators at WCI for IRB approved research purposes if approved by the treating study doctor. Blood samples will be stored indefinitely or until they are used up.

With your permission, any extra blood samples will be stored and used for future research studies by the CTO at WCI. These optional blood samples will also be stored indefinitely or until they are used up. If optional storage and future use is denied or withdrawn by you (submitted in writing to the study doctor), best efforts will be made to stop any additional studies and to destroy your samples.

**RISKS**
The hyperbaric oxygen chamber therapy may cause side effects or other problems. The researchers will be checking your medical information during the study to watch for side effects. However, you should tell the research team about anything that is bothering you or any changes in your health since the last visit. The researchers may be able to take steps to reduce side effects. You may experience none, some, or all of the side effects listed below.

Risks Related to the Hyperbaric Oxygen Chamber Therapy:
When you are placed into the hyperbaric oxygen chamber, you may not feel any changes. However, during certain parts of the treatment, you may experience a sensation of fullness in the ears, similar to the feeling experienced on an airplane. This is a result of the eardrum responding to pressures changes. Prior to treatment, you will be taught a few easy methods to "clear" your ears to avoid discomfort.

The most common side-effects of the HBO chamber therapy include:

- Claustrophobia (having fear or anxiety of enclosed spaces)
- Ear popping.
- Temporary myopia, or nearsightedness (a vision condition in which close objects are seen clearly, but objects farther away appear blurred). If you experience temporary myopia, it might take several weeks to get better.

Rare, but serious risks of the HBO chamber therapy include:

- Lung irritation by the oxygen (This can cause a dry cough, chest tightness, and a decline in lung function. These symptoms may not go away for weeks.
- Seizures, or convulsions (Seizures can be reversed in the chamber by reducing the pressure of oxygen)

Risks Related to Blood Draws:

You will need to have samples of blood taken during the study for laboratory testing. You may experience temporary discomfort from these periodic blood draws. These needle sticks may cause local pain, bruising and swelling, lightheadedness, dizziness and rarely, fainting and/or a local infection.

Risks Related to the Auto-HSPC Transplant and Preparative Treatment Plan:
You have already agreed to receive an Auto-HSPC transplant. The HSPC transplant is a standard clinical procedure for multiple myeloma. All chemotherapy treatments used to prepare you for your transplant are commonly used in Auto-HSPC transplantations as standard of care. A separate consent will be provided to you to describe risks involved for the transplant, including risks involved for the treatment plan used to prepare you for it.

Radiation Risks
The use of the MUGA scan or CT/PET scans might be part of your routine care and you could receive it whether you were in this study or not. There is no additional risk from radiation exposure because you are participating in this study. If you have any concerns about radiation exposure, please ask the study doctor.

**Pregnancy Risks**
The procedures used for your Auto-HSPC transplant might hurt an unborn child or a child who is breast-feeding. If you are a female you cannot be in this study if you are pregnant or nursing a baby. You cannot be in this study if you are trying to get pregnant, or if you are a male and are planning on fathering a child. If you are female, you will have a pregnancy test before the study starts. During the study you must use an approved method of birth control. These include:

- Abstinence (refraining from all acts of vaginal sex)
- Hormonal methods (oral contraceptives, implants or injections)
- Barrier methods (cervical cap with spermicide plus male condom; diaphragm with spermicide plus male condom)
- Intrauterine devices (e.g., Copper T)
- Female tubal sterilization
- Male vasectomy sterilization

The study doctor must approve the form of birth control. You must talk to your study doctor before changing any birth control methods you have already agreed to use.

There may be pregnancy risks that are not known yet. For this reason, you must tell the researcher right away if you get pregnant during the study. If you are male and your female partner becomes pregnant, you must also tell the researcher right away. If a pregnancy occurs while you (or your partner) are participating in this study, the researcher may request information related to the pregnancy including pregnancy details, details of the birth, the presence or absence of any birth defects, and any maternal or newborn complications.

Possibility of Unknown Risks
Because this approach has not been tried before, there may be other side effects or risks that are not yet known. There is a risk that the HBO might lower the efficacy of the transplant treatment.

**NEW INFORMATION**
You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

**BENEFITS**
You might not benefit from this study. If the study therapy is effective, you might benefit from participation. Researchers hope that the information from this research study may be useful in the treatment of other patients who are undergoing an Auto-HSPC transplant.

**ALTERNATIVES**
You can choose not to be in the study. Instead of being in this study, you can receive the preparative treatment plan without the HBO therapy, which is standard procedure for the Auto-HSPC transplant.

The care you receive from your doctor will not be affected in any way, whether or not you decide to be in the study.

**COSTS**
The HBO therapy will be provided free of charge for this study. However, while the HBO therapy is provided free of charge, you and/or your insurance company will be charged for the usual costs associated with preparing and administering standard treatment for the Auto-HSPC transplant and preparative treatment(s). Tests and procedures that are required only for the study but are not a part of your regular medical care will also be provided at no charge.

You or your insurance company will be billed for any standard medical care given during this research study. You will be responsible for any co-pays, insurance deductibles and/or co-insurance required by your health insurance carrier for your standard medical care. This standard medical care includes any care that you would receive for the treatment of your type of cancer whether you were participating in a study or not, such as:

- Routine clinic visits with your doctor or nurse practitioner.
- Tests (Including but not limited to routine items such as: laboratory blood tests, CT, PET/CT, and/or FDG/PET scans, X-rays, lung function, or cardiac testing.)
- Procedures (Including but not limited to routine items such as: bone marrow biopsies and/or aspirates, other tumor biopsies)
- Medications: other standard medications to treat your cancer. This can include other chemotherapies or non-chemotherapy medications used to treat your cancer, and/or medications to treat or prevent side-effects.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study prior to enrolling on a research study. Depending on how your insurance company processes payments for standard medical care given during a research study, you might have unexpected expenses from being in this study. If your insurance company does not pay for your standard medical care, you will be billed for those charges.

Ask your study doctor to discuss the specific costs that will or will not be covered by the sponsor. This

discussion should include who will pay the costs of treating possible side effects.

**FINANCIAL DISCLOSURE**
Funding will be provided by the National Cancer Institute (NCI), which is part of the National Institute of Health (NIH).

**PAYMENT TO SUBJECTS**
You will not be paid for participating in this study.

**COMPENSATION FOR INJURY**
If you are directly injured by the hyperbaric oxygen being studied, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. You will be reimbursed for reasonable and necessary medical costs for such care, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No other funds have been set aside to pay for such things as lost wages or expenses due to a current underlying illness or condition.

If your research injury is paid for by the University, we will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. This information will be used only in accordance with the law. If you are a Medicare beneficiary, information about the study you are in, and any payments made related to your injury, will be reported to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS requirements. This information will not be used for any other purpose.

**University Of Rochester Statement on Access to Information about Your Study Participation in Your Electronic Health Record**

The following information about your study participation will be included in your electronic health record:
- Documenting you are in this study
- A copy of your signed consent form
- Results of all routine testing such as: vital signs, height and weight, ECGs, routine blood tests, CT or MRI scan results, and biopsy results.

The study team may be notified if you receive other health care services at URMC or its Affiliates (e.g., visit to the emergency room). In addition, the following individuals may know you participated in research and may see results of testing conducted for this study:
- Staff at the University of Rochester Medical Center and its Affiliates (e.g., Strong Memorial Hospital, Highland Hospital, URMC primary care, specialist physician offices) who have a reason to access your electronic health record.
- Health care providers who are involved in your care at a facility that is not part of the University of Rochester Medical Center and its Affiliates and who have reason to access your electronic health record.
- Individuals who request a copy of information from your health record for activities such as

treatment or payment (e.g., medical insurance companies, worker's compensation).

**Confidentiality of Records and Authorization to Use and Disclose Information for Research Purposes**

The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will limit access to research databases to only the approved research staff working on the study. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigator for one.

*What information may be used and given to others?*
The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Past and present medical records related to the study
- Results of medical tests

*Who may use and give out information about you?*

- The study doctor and the study staff
- URMC and Affiliates

*Your information may be given to:*

- The Department of Health and Human Services
- The University of Rochester
- The U.S. Food and Drug Administration (FDA) may also need to inspect study records at some point during the study or even after it has been completed. In the event that this should occur, every effort will be made to keep identifying information about you private.

*Why will this information be used and/or given to others?*

- To do the research
- To study the results
- To see if the research was done right

If the results of this study are made public, information that identifies you will not be used.

*What if I decide not to give permission to use and give out my health information?*

- Then you will not be able to be in this research study.

*May I review or copy my information?*

- Yes, but only after the research is over.

*How long will this permission be valid?*

- This permission will last indefinitely.

*May I cancel my permission to use and disclose information?*

- Yes, you may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

*May I withdraw from the study?*

- Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date.
- Information that has already been gathered may still be used and given to others.

*Is my health information protected after it has been given to others?*

- No, there is a risk that your information will be given to others without your permission.

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 website at any time.

**Contact Persons**

For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact**:**

.

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420628, Rochester, NY 14642, for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;
- In the event the study staff could not be reached

**SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY**

You may stop being in the study at any time within the study duration (1 year from the date of transplant). Your decision to stop participation will not prevent you from getting treatment or services at Strong Wound Healing Center, Strong Memorial Hospital or Wilmot Cancer Institute. If you decide to stop the HBO therapy session while in the HBO chamber, the researchers will first need to decrease the pressure

in the chamber until it is returned to a normal level so you are not harmed by stopping the therapy suddenly. You might be asked to come back for a final study visit.

You have the right to cancel your permission for researchers to use your health information. If you want to cancel your permission, please write to Dr. Omar Aljitawi. The mailing address is Dr. Omar Aljitawi, University of Rochester Medical Center, 601 Elmwood Avenue, Box 704, Rochester, NY 14642. If you cancel permission to use your health information, you will be withdrawn from the study. The researchers will stop collecting any additional information about you unless they need information about a side effect of the study device. They may use and share information that was gathered before they received your cancellation.

This study might be stopped, without your consent, by the investigator or by the FDA. Your participation also might be stopped by the investigator if it is in your best interest or if you do not follow the study requirements.

Neither the investigator, nor the University of Rochester Medical Center will be obligated to provide you with the study treatment if the study is stopped early. Your physician will decide about future treatment, if it is needed.

**OPTIONAL STORAGE AND USE OF BLOOD SAMPLES FOR FUTURE RESEARCH:**

As part of this study, we are collecting leftover blood samples from this study. We would like to use these blood samples for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding multiple myeloma cancer, or other diseases and conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur.

We will also share your leftover blood samples with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These investigators may be The University of Rochester, The University of Kansas, at other research centers and institutions, or industry sponsors of research. Specimens will not be labeled with any identifiable information given to other researchers or at the storage location.

If change your mind and do not want us to store and use your blood samples for future research, you should contact the principal investigator identified at the top of this consent form. The blood samples will no longer be used for research purposes. However, if some research with blood samples have already been completed, the information from that research may still be used. Also, if the blood samples have been shared with other researchers, it might not be possible withdraw it to the extent it has been shared

## Optional Data Collection

If you decide to withdraw from the study treatment, we would like to continue to collect information from

you for the study duration or (one year from your transplant date), if you agree. You do not have to agree to the optional continual data collection. Any follow-up data collected for this study will be for the purposes of monitoring side effects that may occur as a result of this trial or for changes related to your cancer progressing.

1.) In the event that you withdraw from the study treatment, will you allow us to continue to collect data for the purposes stated above? Circle either, "Yes" or "No".

Yes No

**Optional Storage and Use of Leftover Blood Samples for Future Research Studies:**

2.) My leftover blood samples may be stored and used for future research as described above. Circle either, "Yes" or "No".

Yes No

**SIGNATURE/DATES**

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study.

**Subject Consent**

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

_____

Subject Name (Printed by Subject)

_____ _____

Signature of Subject Date

I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read the consent before signing.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date

## Schedule of Events

| **HBO+AutoHSPC<br><br>STUDY CALENDAR** | **Screening/ Baseline** | **Day -1** | **Day 0, pre-HBO** | **Day 0 HBO** | **6 hrs Post HBO** | **8 hrs Post HBO** | **Day 1 (24 hrs post HBO)** | **Day 2 and 3 (post HBO)** | **Every Day - Days 1-14 Each Day Post-Transplant** |
|---|---|---|---|---|---|---|---|---|---|
| Approximate Visit Time | | | | | | | | | |
| Informed Consent | X | | | | | | | | |
| Medical History | X | | | | | | | | |
| Concomitant Medication | At each clinical encounter | | | | | | | | |
| Physical Exam (With performance status) | At each clinical encounter | | | | | | | | |
| Adverse Events | At each clinical encounter | | | | | | | | |
| Pregnancy Test | X | | | | | | | | |
| CBC with diff | X | | X | | | | X | X | X |
| MUGA or ECHO | X | | | | | | | | |
| Pulmonary Function Tests | X | | | | | | | | |
| Disease Assessment | X | | | | | | | | |
| High-dose melphalan (Preparative Regimen) | | X | | | | | | | |
| Correlative Blood Samples (EPO, IL-15) | | X | X | | X | X | X | X | |
| HBO Treatment | | | | X | | | | | |
| HSPC Transplant | | | | | X | | | | |
| Acute HBO Toxicity Assessment | | | | | | | X | | |
| Growth factor use days | | | | | | | | | X |

**HBO+AutoHSPC Study Calendar - CONTINUED**

| HBO+AutoHSPC Study Calendar | Day 7 Post - Transplant | First day of neutrophil recovery (+/- 2 days) | Day 15 Post – Transplant (+/- 2 days) | Day 100 Post Transplant | Long-term follow up for PFS<br>1 year post-transplant |
|---|---|---|---|---|---|
| **Medical History** | **Each clinical encounter** | | | | |
| **Concomitant Medication** | **Each clinical encounter** | | | | |
| **Physical Exam (with performance status)** | **Each clinical encounter** | | | | |
| **Vital Signs** | **Each clinical encounter** | | | | |
| **Adverse Events** | **Each clinical encounter** | | | | |
| **Disease Assessment** | | | | **X** | **X** |
| **Research Blood Samples (CBC with diff for ALC Recovery)** | | | **X** | | |
| **Correlative Blood Samples (IL-15, NK cells, EPO )** | **X**** | **X**** | **X** | **X***** | |
| **Study survey** | | | **X******** | | |
| **Duration of hospitalization And readmissions** | **Data will be collected through day +100** | | | | |
| **Blood product transfusions** | **Data will be collected through day +100** | | | | |

*** A window of 3 hours is allowed for post-transplant day 1, 2, and 3 sample collection. If day 7, day 15 or first day of neutrophil recovery sample collection days occur on a weekend or a holiday, the sample is to be collected the first business day after the weekend or holiday.**
**** On day 7 and first day of neutrophil recovery patients will have blood drawn for IL-15 and EPO.**
***** On day 100 patients will have blood drawn for IL-15.**
****** To be completed by patients who completed HBO therapy.**