IRB APPROVED
AS MODIFIED
Aug 07, 2019

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	Autologous, Bone Marrow-Derived Mesenchymal Stem Cell-Derived Neural Progenitor Cells (MSC-NP), Expanded Ex Vivo; Administered Intrathecally
PROTOCOL NO.:	TISCHMS-MSCNP-002 WIRB® Protocol #20162572
PROTOCOL VERSION NO.:	Version 6
INFORMED CONSENT VERSION NO.:	Version 3
SPONSOR:	Tisch MS Research Center of New York
INVESTIGATOR:	Saud A. Sadiq, MD 4TH Floor 521 West 57th Street New York, NY 10019 United States
STUDY-RELATED PHONE NUMBERS:	Saud Sadiq, MD (212) 265-8070 (24 hours)

You are being asked to participate in a stem cell transplant study. Your participation in this study is voluntary. Please take your time and read this Informed Consent Form carefully before you decide whether or not to take part in this research study. Ask the study doctor or a member of the study staff any questions you may have about this study. You can also take a copy of this form home to review with your family and friends. If you have any questions about this study or if you do not understand something in this consent form please ask the study director (Dr. Sadiq at 212-265-8070), the study nurses (Rebecca Mogil, RN or Samantha McKillip, RN at 212-265-8070), the clinical trials manager (Alifiya Tahir at 646-557-3856), or the study coordinators (Madison Clague at 646-557-3852 or Setse Bush at 646-557-3873).

Disclosure of Financial Interests

The Tisch MS Research Center of NY, the sponsor of this study, is providing funds to Dr. Saud Sadiq, principal investigator, on a per subject basis for conducting this research study. The Tisch MS Research Center of NY also owns the patent for the experimental stem cell transplant

process being evaluated in this study. Dr. Sadiq is named as the inventor on that patent and Dr. Harris is named as co-inventor; the patent is under the legal control of the Tisch MS Research Center Board of Directors. Currently no agreements are in place to develop the patent for commercial purposes, nor are there currently or at any time in the past have there been plans for such development. If, in the future, the Tisch MS Research Center of New York Board of Directors determines to develop the patent commercially, Drs. Sadiq and Harris will be entitled to a percentage of the royalties to be determined at that time.

Dr. Sadiq is the Director and Chief Research Scientist of the Tisch MS Research Center of NY and reports to its Board of Directors. He does not any receive any financial compensation for this role.

Why Is This Study Being Done?

You are being asked to participate in this stem cell transplant study because you have moderate to significant disability associated with multiple sclerosis (MS). The purpose of this study is to determine the effectiveness of stem cells (unspecified cells) taken from your body (autologous) as a potential method of repairing the damage to the nerve cells in your brain and spinal cord caused by your disease. This study will use autologous stem cells that are taken from the bone marrow and are called mesenchymal stem cells (MSCs) as a source to possibly repair damaged tissue. These cells taken from the bone marrow will be then manipulated in the laboratory to make them into immature cells that have the ability to differentiate into various forms of mature tissue of the central nervous system. These cells will then be injected back into your spinal fluid.

This study will be done at a single center. Fifty patients will be randomly assigned in equal proportions to either MSCs or placebo (saline). Being randomized (randomly assigned) means that you are put into a group by chance, like flipping a coin. You will have an equal chance of being placed in either group. Neither you, your designated examining neurologist, nor your study coordinators will know which treatment group you are in. In an emergency, this information will be made available.

The stem cells used in this study are cultured over a period of time to develop into immature cells of the central nervous system (Neural progenitor cells). Neural progenitor cells (NPCs) derived from MSCs are an experimental treatment possibility for nerve disorders because of their potential ability to repair damage to the brain. We refer to these stem cells in this document as MSC-NPs.

In our Phase I clinical trial, 20 patients with progressive MS were treated with 3 separate doses of up to 10 million MSC-NPs administered through a spinal tap with doses spaced 3 months apart. Results showed that the doses of the cells were well tolerated, with only minor side effects. These events lasted 24-48 hours post treatment.

The entire study will be done on an outpatient basis, and it is anticipated that no hospitalization should be necessary. This study should not be mistaken for a bone marrow transplant treatment that patients with cancer receive, occasionally referred to as stem cell treatment or stem cell transplant.

Duration of the Study

This study will take approximately 40 months (approximately a little over 3 years) from the screening visit to the end of the follow-up period. You will be randomized (assigned by chance) to either the MSC-NP treatment group or placebo treatment group to start. You will have six rounds of stem cell transplants with MSC-NP's given via spinal tap, at approximately two-month intervals in one year. In an additional year, you will have six rounds of placebo treatments (spinal taps with no MSC-NPs) at approximately two-month intervals. This will happen during the first 2 years of the study. The order of MSC-NP or placebo will depend upon what group you are randomized to. You will not know which group you are in. You will have follow-up appointments at the Tisch Multiple Sclerosis Research Center of New York three months after the 6^{th} and 12^{th} treatments, as well as a 36 month post treatment follow-up visit. You will have up to eighteen visits to the center. It is anticipated that approximately 50 subjects will take part in this study.

What Will Happen in This Study?

If you agree to participate in this stem cell transplant study, you will be expected to come to the Tisch Multiple Sclerosis Research Center at least eighteen times over the course of approximately three years. You will have an MRI's at the beginning of the study, three months after your 6th treatment, three months after your twelfth treatment, and at the 36-month follow up, which will be the end of the study. You will remain on your current MS treatment while you are participating in this trial. In addition, no changes in MS symptom management treatments, orthotic devices, or durable medical equipment will be made during the course of the study. However, if there is clinical improvement, you may discontinue use of MS symptom management treatment, orthotic devices, or durable medical equipment. You will not be able to enroll in any other clinical trials for MS or any other condition while enrolled in this study.

You will also undergo urodynamic testing of bladder function at the beginning of the study, three months following your sixth treatment, and three months following your twelfth treatment. Urodynamic testing is an assessment of how well your bladder and urethra are storing and releasing urine. During urodynamic testing the compliance of the bladder is one of the functions that are measured. Compliance is the ability of the bladder to fill up without any accompanying rise in bladder pressure. You will be instructed to arrive for testing with a full bladder. While you urinate into a container, the volume of urine and the rate at which the bladder empties are measured. A thin, flexible tube (catheter) is then inserted into the bladder through the urethra, and the volume of any urine remaining in the bladder is measured. A slight burning sensation may occur when the catheter is inserted.

Screening Visit (Within Four Months Prior to 1st Treatment)

During your first visit (the screening visit) you will meet with one of the research nurses, the clinical trial manager, or one of the study coordinators, and a designated examining neurologist. The study team will discuss the study with you and answer any questions you may have. If you choose to participate in the study, you will sign this informed consent form. The next step will be a 30-minute visit with a designated examining neurologist, which will be a preliminary screening of your current MS and medical condition and will determine how well you function on a daily basis.

Your designated examining neurologist will evaluate you using the different questionnaires related to your multiple sclerosis and based on how well you function on a daily basis. Your designated examining neurologist will perform a complete physical examination, a complete neurological examination, and other tests that evaluate your nervous system. You will also fill out a questionnaire about any infections you have had. If you are a female and haven't gone through menopause yet, and are not on reliable birth control, a urine or blood pregnancy test will be performed at some point during the screening period. Additionally, a urine sample will be taken to screen for drug and nicotine abuse at some point during the screening period. This is done because use of such substances negatively affects stem cell growth. Due to the importance of this, please note that there could be random drug and nicotine testing done at any point during the study period. If a urine sample tests positive suggesting abuse of drugs, including nicotine, you will be removed from the trial. The screening visit will take approximately 1 hour.

You will also have blood tests which will be done outside the center. A lab slip will be given to you when you are here for the screening visit or sent to you afterwards. These labs include a complete blood count (measures all the cells in your blood), a sedimentation rate test (measures the rate at which red blood cells settle in a test tube), a liver function profile (will test how well your liver functions), a metabolic profile (to see your nutrient level), a thyroid profile (will test how well your thyroid functions), and a coagulation profile (to check if your blood is clotting properly). In addition, you will be required to undergo a panel of infectious disease screening, including a Hepatitis panel (Hepatitis A, B, and C), a test for syphilis (VDRL test), human T-lymphotropic virus (HTLV) I and II, and an HIV test. HIV related information may be shared with other members of the research team besides the principal investigator. If you are found to be HIV positive you will be informed, and you may not participate in this trial. You will be referred to a clinic where you can be treated and counseled. If you test positive for HIV, hepatitis, or syphilis, the results are reported to the state health authorities. All of these tests will make sure you are healthy before you begin the trial. We will have the results of these tests sent to the principal investigator, who will review these results before you come for your second visit to make sure you are still eligible for the study.

Bone Marrow Visit (Within Three Months Prior to 1st Treatment)

At your second visit (the bone marrow visit) you will have vitals taken in addition to the bone marrow aspiration procedure.

You will have a sample of bone marrow taken from your sternum (chest bone) or hip bone. Dr. Gabriel Sara, a board=certified hematologist, will remove a portion of your bone marrow using a needle. You will be given a local numbing agent, and a thin needle with a syringe attached will be inserted into your chest bone. The sample of bone marrow, which is approximately two tablespoons of a blood like liquid, will be taken by a needle and immediately sent to the laboratory where the NPCs will be taken out. The bone marrow procedure itself takes less than 15 minutes and takes place at the IMSMP. The entire visit will take approximately 2 hours. Bone marrow samples from subjects who have previously had bone marrow harvested (portion removed) at IMSMP may be used for implantation as long they are deemed acceptable for use. This applies to bone marrow harvested prior to enrollment in this study.

Baseline Visit (Within 1 Month Prior to 1st Treatment)

You will need to have additional testing done within one month prior to starting treatment. You will have three MRI's performed. These tests look at images of your brain, cervical spine (neck), and thoracic spine (upper and middle back). You may have a visit with your designated examining neurologist (if not already done earlier in the screening period or if scheduling indicates) who will perform a complete physical exam, a complete neurological exam, and other tests that evaluate your nervous system and determine how well you function on a daily basis.

You will fill out some questionnaires about your bladder, your walking and headaches. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). You will also undergo urodynamic testing performed outside of the center to determine how well your bladder is functioning. A urine sample will also be collected to screen for UTIs (urinary tract infections).

Treatment Phase

Patients Receiving MSC-NP in Year 1

Your first MSC-NP treatment will occur at least three months after your bone marrow visit. It may be sooner if you have already had your bone marrow harvested prior to enrolling in this study. If you are in this group (you will not be aware of which treatment group you are in), Dr. Sadiq will inject cells into the area below your spinal cord through a needle in your back; this is called an intrathecal (IT) injection. The procedure for this is identical to that done of a routine spinal tap. A small amount of cerebrospinal fluid and blood will be withdrawn for laboratory analysis. Some of this fluid will be stored in the laboratory for future analysis. As an extra

precaution against infections, you will be given IV (intravenous) antibiotics through your arm. This visit will take approximately 5 hours.

You will be asked to take Tylenol every 6 hours for two days after each MSC-NP treatment.

The next five MSC-NP treatments will occur every two months. The procedure will be the same as indicated above. Prior to the fourth MSC-NP treatment, you will be evaluated by your designated examining neurologist and you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). Follow up phone calls to transplant visits will take place according to the same schedule for each MSC-NP treatment.

In the week following each MSC-NP treatment, you will have two phone conversations with either one of the study nurses, the clinical trials manager, a study coordinator, or with your designated examining neurologist. These phone calls will occur 2 days, 7 days, and 1 month after the treatment. These calls will last approximately 10 minutes, but they make take longer if you have had symptoms. You will be asked if you had a headache or other side effects and will complete a questionnaire if you have had a headache. These phone calls are to monitor your safety and make sure that the study team knows what you are experiencing.

Three months after your sixth MSC-NP treatment you will come to the center to be evaluated by your designated examining neurologist. They will review your body systems and complete questionnaires. During this time, you will also schedule MRI's of the brain, cervical spine, and thoracic spine. The MRI results will be sent to a board certified neuroradiologist (who will be blinded to the study) for review. Along with the MRI's, urodynamic testing will need to be set up at this time point. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). A urine sample will also be collected to screen for a UTI (urinary tract infection).

One month after this, you will begin the placebo treatment phase of the trial (you will not be aware of which treatment group you are in). This procedure will be the same as before, only without the intrathecal (IT) injection of your cells. Dr. Sadiq will still perform a routine lumbar puncture (spinal tap) to imitate MSC-NP treatment, however, you will only be injected with preservative-free sterile saline, and not actually be given any MSC-NP's. A small amount of cerebrospinal fluid and blood will be withdrawn for laboratory analysis. Some of this fluid will be stored in the laboratory for future analysis. As an extra precaution against infections, you will be given IV (intravenous) antibiotics through your arm. This visit will take approximately 5 hours.

The next five placebo treatments will occur every two months. Again, Dr. Sadiq will perform a routine lumbar puncture (spinal tap) to imitate MSC-NP treatment; however, you will not actually be given any MSC-NP's. The procedure will be the same as indicated above. Prior to the fourth placebo treatment, you will be evaluated by your designated examining neurologist and you will participate in testing to determine your abilities in walking, memory, and dexterity

(ability to use your hands). Follow up phone calls to these visits will take place according to the same schedule for each placebo treatment.

In the week following each placebo treatment, you will have two phone conversations with either one of the study nurses, the clinical trials manager, a study coordinator, or with your designated examining neurologist. These phone calls will occur 2 days, 7 days, and 1 month after the treatment. These calls will last approximately 10 minutes, but they make take longer if you have had symptoms. You will be asked if you had a headache or other side effects and will complete a questionnaire if you have had a headache. These phone calls are to monitor your safety and make sure that the study team knows what you are experiencing.

Three months after your sixth placebo treatment you will come to the center to be evaluated by your designated examining neurologist. They will review your body systems and complete questionnaires. A spinal tap will be performed, and a small amount of cerebrospinal fluid and blood will be withdrawn for laboratory analysis. Some of this fluid will be stored in the laboratory for future analysis.

During this time, you will also schedule MRI's of the brain, cervical spine, and thoracic spine. The MRI results will be sent to a board certified neuroradiologist (who will be blinded to the study) for review. Along with the MRI's, urodynamic testing will be need to be set up at this time point. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). A routine urine sample will also be collected to screen for a UTI (urinary tract infection).

If you have an intrathecal Medtronic pump installed for spasticity and pain management, you will be given the MSC-NPs through the pump. MSC-NPs will be administered through the side port of the pump. The treating physician will apply betadine to the area of the pump. A sterile drape is then placed over the region to create the procedure field. The side port will then be accessed with a needle (similar to a routine side port pump procedure). Before administering any MSC-NPs, the side port catheter will be aspirated to clear any drug in path. After the MSC-NPs are injected through the side port, extra saline will be flushed through to make sure that the MSC-NPs have been cleared out of the side port catheter. Following the procedure, a prime bolus will be administered via Medtronic programmer to ensure continuous supply of your medicine.

Patients Receiving Placebo in Year 1

Your first placebo treatment will occur at least three months after your bone marrow visit. It may be sooner if you have already had your bone marrow harvested prior to enrolling in this study. If you are in this group (you will not be aware of which treatment group you are in), Dr. Sadiq will inject cells into the area below your spinal cord through a needle in your back; this is called an intrathecal (IT) injection. The procedure for this is identical to that done of a routine spinal tap. A small amount of cerebrospinal fluid and blood will be withdrawn for laboratory

analysis. Some of this fluid will be stored in the laboratory for future analysis. As an extra precaution against infections, you will be given IV (intravenous) antibiotics through your arm. This visit will take approximately 5 hours.

The next five placebo treatments will occur every two months. Dr. Sadiq will perform a spinal tap to imitate MSC-NP treatment, however, you will only be injected with preservative-free sterile saline, and not actually be given any MSC-NP's. The procedure will be the same as indicated above. Prior to the fourth placebo treatment, you will be evaluated by your designated examining neurologist and you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). Follow up phone calls to these visits will take place according to the same schedule for each placebo treatment.

In the week following each placebo treatment, you will have two phone conversations with either one of the study nurses, the clinical trials manager, a study coordinator, or with your designated examining neurologist. These phone calls will occur 2 days, 7 days, and 1 month after the treatment. These calls will last approximately 10 minutes, but they make take longer if you have had symptoms. You will be asked if you had a headache or other side effects and will complete a questionnaire if you have had a headache. These phone calls are to monitor your safety and make sure that the study team knows what you are experiencing.

Three months after your sixth placebo treatment you will come to the center to be evaluated by your designated examining neurologist. They will review your body systems and complete questionnaires. During this time, you will also schedule MRI's of the brain, cervical spine, and thoracic spine. The MRI results will be sent to a board certified neuroradiologist (who will be blinded to the study) for review. Along with the MRI's, urodynamic testing will need to be set up at this time point. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). A urine sample will also be collected to screen for a UTI (urinary tract infection).

One month after this, you will begin the MSC-NP treatment phase of the trial (you will not be aware of which treatment group you are in). Dr. Sadiq will inject cells into the area below your spinal cord through a needle in your back; this is called an intrathecal (IT) injection. The procedure of doing this is identical to that done of a routine lumbar puncture (spinal tap). Before the transplant, a small amount of cerebrospinal fluid and blood will be withdrawn for laboratory analysis. Some of this fluid will be stored in the laboratory for future analysis. As an extra precaution against infections, you will be given IV antibiotics through your arm. This visit will take approximately 5 hours.

The next five MSC-NP treatments will occur every two months. The procedure will be the same as indicated above. Prior to the fourth MSC-NP treatment, you will be evaluated by your designated examining neurologist and you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). Follow up phone calls to transplant visits will take place according to the same schedule for each MSC-NP treatment.

In the week following each MSC-NP treatment, you will have two phone conversations with either one of the study nurses, the clinical trials manager, a study coordinator, or with your designated examining neurologist. These phone calls will occur 2 days, 7 days, and 1 month after the treatment. These calls will last approximately 10 minutes, but they make take longer if you have had symptoms. You will be asked if you had a headache or other side effects and will complete a questionnaire if you have had a headache. These phone calls are to monitor your safety and make sure that the study team knows what you are experiencing.

Three months after your sixth MSC-NP treatment you will come to the center to be evaluated by your designated examining neurologist. They will review your body systems and complete questionnaires. A spinal tap will be performed, and a small amount of cerebrospinal fluid and blood will be withdrawn for laboratory analysis. Some of this fluid will be stored in the laboratory for future analysis.

During this time, you will also schedule MRI's of the brain, cervical spine, and thoracic spine. The MRI results will be sent to a board certified neuroradiologist (who will be blinded to the study) for review. Along with the MRI's, urodynamic testing will be need to be set up at this time point. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands). A urine sample will also be collected to screen for UTIs (urinary tract infections).

Final Study Follow-Up Visit

The final follow-up office visit will happen 3 years after your first treatment visit. You will come to the center to be evaluated by your designated examining neurologist. They will review your body systems and complete questionnaires. During this time, you will also schedule MRI's of the brain, cervical spine, and thoracic spine. The MRI results will be sent to a board certified neuroradiologist (who will be blinded to the study) for review. In addition, you will participate in testing to determine your abilities in walking, memory, and dexterity (ability to use your hands).

Cerebrospinal fluid and blood specimen collection for research

Cerebrospinal fluid (CSF) and blood specimens will be collected at each of the 12 spinal taps and also during the follow up visit 3 months after the end of your second treatment year. At each of these visits, the treating neurologist will withdraw one tube (2 teaspoons) of CSF during the spinal tap. Also 2 tubes (2-3 teaspoons) of blood will be collected from your vein. All blood and CSF samples will be processed in the research laboratory at Tisch MSRCNY and may be stored for up to 15 years. All laboratory work will be conducted using a de-identified label specific for your sample, which will not contain any personal markers such as date of birth or name. A record of labels as they correspond to individuals' samples will be kept confidential in a locked file cabinet at Tisch MSRCNY. Only key research personnel will have access to this information.

Your name will not be reported in any publication or results of the study; only the data obtained as a result of your participation in this study will be made public. All specimens will be used for research purposes to investigate biological markers that can help understand the progression of the disease and the response to this experimental therapy.

What Are the Risks and Discomforts of Being in This Study?

Transplant Risks

Risks associated with NPCs are infection and uncontrolled cell growth. Uncontrolled cell growth may lead to cancer. All NPCs will be tested for infection in multiple ways and for uncontrolled growth before they are injected into you. All the procedures are done with full standard precautions to help minimize risk of infections. As mentioned above, you will be given antibiotics with each stem cell injection. There is a possible risk associated with these antibiotics if you have an unknown allergy. Less common side effects include kidney failure, deafness, localized skin reactions, and change in blood pressure, among other possible reactions.

Since these stem cells come from your bone marrow, they are autologous (obtained from your own cells), and there is no risk of your body rejecting them. This should also not affect your ability to fight off infection. You may experience headache or fever; however, these side effects are not expected to last longer than a few days. Follow up phone calls will assess if you are experiencing either of these symptoms.

Another transplant risk is developing severe infection or septic meningitis. The symptoms of septic meningitis include headache, neck stiffness, nausea, vomiting, and fever. If you develop any changes in your thinking or thought process (cognitive function), such as memory loss, difficulty finding words, or difficulty expressing yourself, contact the study doctor immediately. There is a possibility of death or irreversible brain damage from meningitis.

There is a slight risk of side effects that could occur due to growth factor contamination of the cells being injected. This could cause tumors and other unknown effects.

Although the study was designed to minimize the risks stated above, they cannot be eliminated entirely.

Risk of Intrathecal Injection

There are risks associated with the spinal tap: You may experience some pain, which will be minimized with the use of a numbing agent in the area. About 50% of subjects get a post-puncture headache with the standard spinal tap and these may last 3-7 days. However, the type of needle we use for this study can reduce the incidence of spinal headaches to less than 10%. Spinal headaches are characterized by severe, constant head and neck ache that gets worse

when you are upright. This type of headache may also cause vomiting. If you think you have a spinal headache, you should lie absolutely flat and drink as many clear liquids as you can tolerate. If the headache is not gone or has not improved in 48hrs, please call our office to arrange for a blood patch. Fewer than 5% of subjects experience a severe headache that may require treatment (a blood patch). Blood patches are performed by an anesthesiologist at a hospital for treatment of spinal headaches and nausea that sometimes follows a spinal tap. The blood patch procedure consists of an injection at the spinal tap site of a small quantity of your own blood. The introduction of this blood acts to patch the hole in the outer cover of the spinal cord that was created by the needle at the time of the spinal injection.

A risk of bleeding has been associated with lumbar puncture procedure among patients suffering from blood coagulation disorders. If you satisfy the inclusion and exclusion criteria for participation in this trial, you do not suffer from a blood coagulation disorder.

Using an intrathecal pump to deliver the cells may increase the risks of pump problems and has unknown risks.

Risk of Bone Marrow Sample Removal

There are risks associated with bone marrow sample removal. During the procedure, you may experience a stinging sensation from the anesthetic injection. Some people feel brief, sharp pain as the marrow is being removed. After the procedure you may experience pain or discomfort at the collection site. Common side effects also include fatigue and low back pain. A small percentage of subjects (0.1-0.3%) experience serious complications such as a reaction to anesthesia. Bone fracture has also been reported. There is a risk of putting a hole in the aorta, the major blood vessel carrying blood from the heart, during removal of bone marrow from the sternum (chest area).

A risk of bleeding has been associated with bone marrow aspiration procedure among patients suffering from blood clotting disorders. If you satisfy the inclusion and exclusion criteria for participation in this trial, you do not suffer from a blood clotting disorder.

MRI Risks

There is a risk of claustrophobia associated with undergoing an MRI exam. You will need to lie quietly in a tunnel that is 6 ft. by 2.5 ft. for approximately 90 minutes. During the MRI you will always be able to communicate with doctors. If you wish to be removed from the MRI machine, a doctor or technician will do so immediately. Due to the nature of the MRI machine, you should not participate in the study if you have metal implants in your body.

Urodynamic Testing Risks

Urodynamic testing of bladder compliance (ability of the bladder to fill up without an accompanying rise in bladder pressure) carries a risk of occasional discomfort and a small risk of urinary tract infection.

Risks of Blood Drawing

During this study, your blood will be drawn to perform a variety of tests. The risks of drawing blood include temporary discomfort from the needle in your arm, bleeding, bruising, swelling at the needle site, fainting, and, in rare instances, infection.

Risks of Antibiotics

During each transplant or placebo procedure, you will receive an IV infusion of two antibiotics, Tobramycin and Vancomycin. Because you will receive only a single dose of each antibiotic at each transplant it is unlikely that you will experience any of the side effects normally associated with these antibiotics, such as nausea, vomiting or diarrhea. During the infusion of vancomycin, you may experience some flushing. The research nurse will continuously monitor you during infusion to prevent flushing. An allergic reaction to the antibiotics is possible. The research nurse will monitor for allergic reactions and stop the infusion if this happens.

Tylenol Risks

Side effects of Tylenol include: nausea, stomach pain and loss of appetite,

Unknown Risks

You might experience side effects or discomforts that are not listed in this form. Some side effects may not be known yet. It is possible that you will be the first subject to experience a particular effect. For more information about side effects and risks, ask your study doctor. Tell the study doctor or study staff right away if you think you are experiencing a side effect or have any problems.

Pregnancy/Birth Control

The risks of this transplant and the associated research procedures to a fetus are unknown. You cannot participate in this study if you are a woman who is pregnant, nursing, or planning on becoming pregnant during the course of the study. If you are of childbearing potential, you may enter this study only if you are practicing a medically approved, effective method of birth control, such as hormonal contraceptives, intrauterine device, or spermicide and barrier (for example, condom or diaphragm), or you are practicing abstinence. If you become pregnant

during the study, you must notify the study doctor immediately. Your treatment will be terminated, but you will continue to be monitored for safety for the rest of the study.

Benefits

The purpose of this study is to determine the effectiveness of stem cells as a potential method of repairing the damage to the nerve cells of your brain and spinal cord caused by multiple sclerosis. There is objective data from our Phase I trial suggesting that this treatment may lead to improvement, however, this must be confirmed through a placebo-controlled trial. A placebo-controlled trial is a study where some subjects receive the actual treatment and some receive a placebo, which in this study is a saline injection. Your participation in this study may be beneficial to other patients with MS in the future.

What Are the Alternatives to Being in this Study?

You may choose to not participate in this study. Stem cell mediated repair is not a standard treatment for MS and is not available outside of a research study. You could participate in other studies involving drug treatments that are being studied to slow down the disease, such as the use of Rituxan (Rituximab). In addition, you could use the many FDA approved treatments for MS. These include: Avonex (interferon beta 1-a), Betaseron (interferon beta 1-b), Copaxone (glatiramer acetate), Glatopa (glatiramer acetate – generic equivalent of Copaxone 20mg dose), Rebif (interferon beta 1-a), Novantrone (Mitoxantrone), Extavia (interferon beta-1b), Plegridy (peginterferon beta-1a), Aubagio (teriflunomide), Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Lemtrada (alemtuzumab), Tysabri (natalizumab), and Ocrevus (ocrelizumab). There are very limited FDA-approved treatments for secondary progressive MS (SPMS) and primary progressive MS (PPMS). Other options are to try out treatments that are unapproved for SPMS or PPMS (but that are approved for other MS types), to enroll in another experimental trial, or to receive no treatment. You should discuss these options with your doctor.

Costs

All costs for this study will be covered by the Tisch Multiple Sclerosis Research Center of New York. This includes the cost of the bone marrow procedure; all study treatments, MRIs, and any offsite testing. The Tisch Multiple Sclerosis Research Center of New York (TMSRCNY) will not reimburse patients for travel costs or food. During the course of the study, non-research related medical costs will not be covered.

Compensation for Injury

If you are injured as a result of your participation in this research study, medical care to treat such injury will be made available to you. The cost associated with the treatment of such injury will be covered by TMSRCNY.

No other compensation will be offered by the Tisch Multiple Sclerosis Research Center of New York.

By signing this form, you are not waiving any legal rights to seek additional compensation through the courts.

Will You Be Paid for Being in This Study?

You will not be paid for your participation in this study. Information learned from this study may be used to develop commercial products, and you will not receive any share of the profits from such commercial products.

Will You Be Told of Any New Information?

During the course of the study, if new information becomes available that may affect your decision to continue participating in the study, you will be informed of this information.

Confidentiality

To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be maintained by TMSRCNY and submitted to the U.S. Food and Drug Administration (FDA). Medical records, which identify you and the consent form signed by you, will be looked at by TMSRCNY personnel assigned to do so by the Principal Investigator, and may be looked at by the FDA and other regulatory agencies, and the Western Institutional Review Board. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/or publications.

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.

Confidentiality of Biological Specimens Stored for Future Research and Analysis

All specimens (bone marrow stem cells, blood serum/plasma, and cerebrospinal fluid) will be stored in a secured freezer at TMSRCNY. To maintain confidentiality, all samples will be coded with a unique identifier that is not traceable to the study subject's personal information except by the designated TMSRCNY study investigator. Samples may be stored at TMSRCNY indefinitely for further analysis that is related to the study outcome. As a participant in the study, you are giving consent to TMSRCNY to use the above-mentioned specimens for any analysis the institution deems necessary for research purposes after the end of this study.

Who has the authorization to use and disclose my protected health information?

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

- ***Past and present medical records***
- ***Research records***
- ***Records about phone calls made as part of this research***
- ***Records about your study visits***
- ***Information obtained during this research about laboratory test results***
- ***Results from diagnostic and medical procedures including, but not limited to, imaging, physical examinations and medical history, and***
- ***Billing records.***

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Your information may be given to the Sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the Sponsor or are owned by the Sponsor.

Information about you and your health which might identify you may be given to:

- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Western Institutional Review Board
- Accrediting agencies

- Data Safety Monitoring Boards
- Health Insurers/Payers

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health confidential.

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The Sponsor will analyze and evaluate the results of the study. In addition, people from the Sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the Sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This Authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you chose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any affect on your medical care, and you will not lose any benefits or legal rights to which you are entitled.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, 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.

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (212) 480-2493 or the New York City Commission of Human Rights at (212) 306-7450. These agencies are responsible for protecting your rights.

Voluntary Participation/Withdrawal

Your decision to participate in this study is completely voluntary. Refusal to participate in this study will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from the study at any time and withdrawal will not result in penalty or loss of medical benefits to you. Any significant results that develop during the course of the study will be explained.

Dr. Sadiq or the Sponsor may end your participation in this study without your consent at any time, for any reason, including: if it is in your best interest or if you do not consent to continue in the study after being told of changes in the research that may affect you. You also may be withdrawn if you become pregnant or incarcerated.

If you stop being in this study, you will still need to see your designated examining neurologist for several appointments. You will have the phone conversations after each treatment as described above. You will also have appointments at 3 months after your last treatment and 36 months after your initial treatment as if you were participating in the study.

Whom to Contact

During the course of this clinical study, if you have any further questions, concerns, complaints or research related injuries as a result of your participation, please contact Dr. Saud A. Sadiq, MD, at 212-265-8070 (24 hours).

If you have any questions about your rights as a research subject or questions, concerns, input or complaints regarding this research study, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent reviews of research.

WIRB will not be able to answer some study specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or you wish to speak to someone other than the research staff.

PARTICIPANT'S CONSENT STATEMENT:

I have read the previous page(s) of the consent form. I understand that I am free to ask additional questions, and all of my questions have been answered to my satisfaction.

If I want additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact Dr. Saud A. Sadiq at 212-265-8070.

I understand that participation in this study is voluntary, and I may refuse to participate or may discontinue participation without penalty, loss of benefits, or prejudice to the quality of care that I will receive.

None of my legal rights are being waived by signing this form.

I acknowledge that participation in this study is completely voluntary. I consent to participate in the study.

_____
Subject's Name (Printed)

_____ _____
Subject's Signature Date

_____
Name of Person Obtaining Consent (Printed)

_____ _____
Signature of Person Obtaining Consent Date

The contents of this consent form were verbally presented to the subject and all questions were completely answered. In the future, I will continue to answer all subject questions regarding this study to the best of my ability. The subject will receive a copy of the consent form.

_____ _____
Physician/Investigator Date