Randomized Double-Blind Placebo-Controlled Adaptive Design Trial Of Intrathecally Administered Autologous Mesenchymal Stem Cells In Multiple System Atrophy

NCT05167721

May 30, 2025

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Randomized Double-Blind Placebo-Controlled Adaptive Design Trial Of Intrathecally Administered Autologous Mesenchymal Stem Cells In Multiple System Atrophy

IRB#: 21-005569

Principal Investigator: Dr. W. Singer and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to find out if stem cells harvested from your own fatty tissue and expanded in a laboratory to high numbers can slow down disease progression in multiple system atrophy (MSA) patients when injected into the fluid that surrounds your brain and spinal cord. You have been asked to take part in this research because you have been diagnosed with MSA.
What's Involved	Study participation involves up to 11 in-person study visits and 2 phone follow-up visits over the course of up to 18 months. Various tests and assessments are done at different time-points that include review of your medical history and current medications, vital signs, physical examinations, questionnaires, blood draws, collection of spinal fluid via spinal tap, and MRI scans of the brain and lumbar spine. There will be a fat biopsy to collect your stem cells.

	There will be 4 study treatments which require observation in our Clinical Research and Trials Unit and consist of injection of stem cells or placebo into the spinal fluid via lumbar puncture. You will be randomized (like drawing straws) to receive active treatment (stem cells) versus placebo only. Two out of 3 participants will receive active treatment.
Key Information	Important risks to consider include possible changes to the nerves in the area of the stem cell injection that can sometimes cause low back and thigh pain; headache; fever; and risks that are not yet known. There are a number of study visits and interventions which can be time consuming, and some can cause discomfort. The study intervention may not make your health better. You will not need to pay for study tests and procedures. You do not have to be in this study to receive treatment for your condition. You should talk to the researcher and your physicians about your choices before you decide if you will take part in this study.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Dr. Wolfgang Singer **Phone:** (507) 284-2511 **Study Team Contacts:** Toni Gehrking **Phone:** (507) 284-4462 Jennifer Anderson **Phone:** (507) 284-2090 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have been diagnosed with Multiple System Atrophy (MSA). About 76 people will take part in this research study at Mayo Clinic.

Why is this research study being done?

The purpose of this study is to find out if stem cells harvested from your own fatty tissue (mesenchymal stem cells, MSCs) and expanded in a laboratory to high numbers can slow down disease progression in MSA patients when injected into the cerebrospinal fluid (CSF, which is the fluid that surrounds your brain and spinal cord). We also want to find out if injecting MSCs into the CSF is safe and well tolerated. The study is based on previous studies that showed positive effects when using this approach without significant adverse effects. MSCs are a type of stem cell that can grow into a number of different kinds of cells.

The use of MSCs is considered investigational, which means it has not been approved by the Food and Drug Administration (FDA) for routine clinical use. However, the FDA has allowed the use of mesenchymal stem cells in this research study.

Information you should know

Who is Funding the Study?
The United States Food and Drug Administration (FDA) and Mayo Clinic are funding this study.

Information Regarding Conflict of Interest:
This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and is being conducted in compliance with Mayo Clinic Conflict of Interest policies.

Both the Mayo Clinic Conflict of Interest Review Board and the Institutional Review Board have reviewed the Financial Conflict of Interest for one or more of the investigators and/or Mayo Clinic related to this research and they have determined that this Financial Conflict of Interest poses no additional significant risk to the welfare of participants in this research project or to the integrity of the research.

Additional information is available to any interested study participant regarding the details of this Financial Conflict of Interest and how it is being managed by contacting the study coordinator or the Office of Conflict of Interest Review at 507-284-0075.

One or more of the investigators associated with this project and Mayo Clinic have a Financial Conflict of Interest in technology used in the research and the investigator(s) and Mayo Clinic may stand to gain financially from the successful outcome of the research.

Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in the study for up to 18 months.

What will happen to you while you are in this research study?

If you agree to be in the study, you will be asked to participate in the following:

Screening Visit
At your first study visit, also called the Screening visit, we will:

- ask questions about your symptoms, limitations, and your medical history,
- have you undergo a physical and mental status examination and a review of your current medications,
- have blood drawn (approximately 1 tablespoon).
    - If you are a woman and can become pregnant, we will also collect urine for a pregnancy test.

Fat Biopsy
Following screening procedures as above, and once it is determined that you can safely participate in the study, you will undergo a fat biopsy to harvest stem cells.

A fat biopsy is done through a small (1-2 inch) cut in your abdomen or thigh, where less than a teaspoon of fat is removed from under the skin. The actual site of the biopsy will be determined at the time of the biopsy. This procedure will be done by a qualified health professional during an outpatient visit. You will be given a local anesthetic to numb the site where the biopsy will be taken. The biopsy site will be closed using stitches that are absorbed by the body. The stitches are usually reabsorbed in one to three weeks. You will be given instructions on how to care for your biopsy site.

There is a possibility that the cells from the fat tissue removed during the biopsy may not grow. If this happens, a second biopsy will be done. Under very rare circumstances, a third biopsy may be necessary in order to grow the required number of cells. However, if the third biopsy sample does not grow cells, no further biopsies will be done, and you will not continue with the study.

Baseline Visit and First Study Product Administration (Week 0, approximately 2 months after the fat biopsy)
During this visit, the following tests and procedures will be performed:

- Re-confirmation of MSA diagnosis
- Recording of current medications
- Recording of vital signs & height/weight
- Complete neurologic examination
- General medical examination
- UMSARS (an assessment completed by a study physician based on questions about your disease and exam findings)
- COMPASS Select (a questionnaire about some of your symptoms)
- MRI of the brain and lumbar spine
- Blood draw (about 2 tablespoons)

You will then undergo study treatment and observation at the Clinical Research Unit at Mayo Clinic Rochester. You will stay there for at least 4 hours after receiving the study treatment.

You will have a saline lock placed in your arm. This is similar to having an intravenous line (IV). This is a safety measure in case we need to give you IV fluids or medications in an emergency.

You will be randomly assigned (like drawing straws) to receive either the active study treatment (mesenchymal stem cells) four times, the active study treatment two times, or no active study treatment (placebo in the form of a water/salt solution, called lactated Ringers). As part of this study, you will receive 4 study treatments; one will occur at this study visit, the other treatments will be at the 3, 6, and 9-month visits.

One group of patients will receive mesenchymal stem cells at each of these visits; another group of patients will receive mesenchymal stem cells at baseline and at 6 months only and receive placebo at the 3 and 9 month visits; and another group of patients will receive placebo at all 4 of these visits.

The randomization is done so you have a 2:1 chance to receive one of the active treatments (out of 3 people, 2 get the active treatment and 1 the placebo only). Neither you nor your study doctors will know or can influence which treatment you will receive.

At the time of the injection, the mesenchymal stem cells that were grown from your fat biopsy or placebo will be injected into your spinal fluid with a needle placed in your lumbar spine (lower back) in a process similar to a spinal tap. This will be done by a trained health professional. You will remain in a regular hospital bed for the procedure. During the procedure, a sample of your spinal fluid (about 2 tablespoons) will also be collected.

After the procedure, the bed will be placed in a slight head-down position, and you will be gently rotated from side to side every 15 minutes for two hours to maximize the even distribution of the stem cells or placebo solution. You will have your blood pressure, heart rate, temperature, and breathing measured every 15 minutes for one hour, and then every hour until you are discharged. You will also be assessed for pain and any other adverse effects. A physician will discuss any potential problems or adverse effects with you. This physician is specifically assigned to discuss and manage any adverse events you may experience. Please discuss adverse events only with that physician who you will meet repeatedly during the study and whose contact information you will receive. Please do not discuss adverse events with the doctors evaluating your MSA and its progression to make sure they remain blinded to your treatment assignment.

Two hours after the injection, you will be able to get out of bed, sit in a chair, and walk around. You can also take your regular medications. At the time of discharge, you will be provided phone numbers and instructions should you need to contact the study team with any questions or concerns.

1-week Follow-up Visit (Week 1)
About 1 week after your study treatment, you will have a follow-up visit at the out-patient Clinical Research Unit at Mayo Clinic Rochester. At this visit, the following tests and procedures will be completed:

- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- Documentation of adverse events
- About 2 tablespoons of blood will be drawn

- You will also have a spinal tap to collect spinal fluid (about 2 tablespoons) to test for any reactions to the study treatment.

You will meet with the study physician assigned to assess adverse events. Any problems you may have encountered following the study treatment will be discussed.

3-month Follow-up Visit and Second Study Product Administration (Week 13)

The following tests and procedures will be performed:

- Documentation of adverse events
- Recording of current medications
- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- UMSARS
- Blood draw (about 2 tablespoons)

You will meet with the study physician assigned to assess adverse events who will discuss with you any adverse effects you may have experienced as a result of your treatment (stem cells or placebo) and the physician will determine if it is safe for you to have another treatment, or if it is not safe to proceed. If it is decided that it is safe to proceed, you will again undergo study treatment and observation at the Clinical Research Unit at Mayo Clinic Rochester. You will stay there for at least 4 hours after receiving the study treatment. and undergo the same procedures as with the first injection. Please do not discuss adverse events with the doctors evaluating your MSA and its progression to make sure they remain blinded to your treatment assignment.

1-week Follow-up Visit (Week 14)

You will receive a follow-up phone call from the study physician assigned to assess adverse events about 1 week after the study treatment. Any problems you may have encountered following the study treatment will be discussed.

6-month Follow-up Visit and Third Study Product Administration (Week 26)

During this visit, the following tests and procedures will be performed:

- Documentation of adverse events
- Recording of current medications
- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- UMSARS

- COMPASS Select
- Blood draw (about 2 tablespoons)

You will meet with the study physician assigned to assess adverse events who will discuss with you any adverse effects you may have experienced as a result of your treatment (stem cells or placebo), and the physician will determine if it is safe for you to have another treatment, or if it is not safe to proceed. If it is decided that it is safe to proceed, you will again undergo study treatment and observation at the Clinical Research Unit at Mayo Clinic Rochester. You will stay there for at least 4 hours after receiving the study treatment. and undergo the same procedures as with the first injection. Please do not discuss adverse events with the doctors evaluating your MSA and its progression to make sure they remain blinded to your treatment assignment.

1-week Follow-up Visit (Week 27)
About 1 week after your study treatment you will have a follow-up visit at the out-patient Clinical Research Unit at Mayo Clinic Rochester. At this visit, the following tests and procedures will be completed:

- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- Documentation of adverse events
- About 2 tablespoons of blood will be drawn
- You will also have a spinal tap to collect spinal fluid (about 2 tablespoons) to test for any reactions to the study treatment.

9-month Follow-up Visit and Fourth Study Product Administration (Week 39)
The following tests and procedures will be performed:

- Documentation of adverse events
- Recording of current medications
- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- UMSARS
- Blood draw (about 2 tablespoons)

You will meet with the study physician assigned to assess adverse events who will discuss with you any adverse effects you may have experienced as a result of your treatment (stem cells or placebo) and the physician will determine if it is safe for you to have another treatment, or if it is not safe to proceed. If it is decided that it is safe to proceed, you will again undergo study treatment and observation at the Clinical Research Unit at Mayo Clinic Rochester.

You will stay there for at least 4 hours after receiving the study treatment. and undergo the same procedures as with the first injection. Please do not discuss adverse events with the doctors evaluating your MSA and its progression to make sure they remain blinded to your treatment assignment.

1-week Follow-up Visit (Week 40)
You will receive a follow-up phone call from the study physician assigned to assess adverse events about 1 week after the study treatment. Any problems you may have encountered following the study treatment will be discussed.

12-month (week 52) Follow-up Visit (Week 52)
During this visit, the following tests and procedures will be performed:

- Documentation of adverse events
- Recording of current medications
- Recording of vital signs & weight
- Complete neurologic examination
- General medical examination
- UMSARS
- COMPASS Select
- Blood draw (about 2 tablespoons)
- MRI of the brain and lumbar spine (this MRI of the lumbar spine will require a contrast dye called Gadolinium, which will be injected in a vein on your arm)

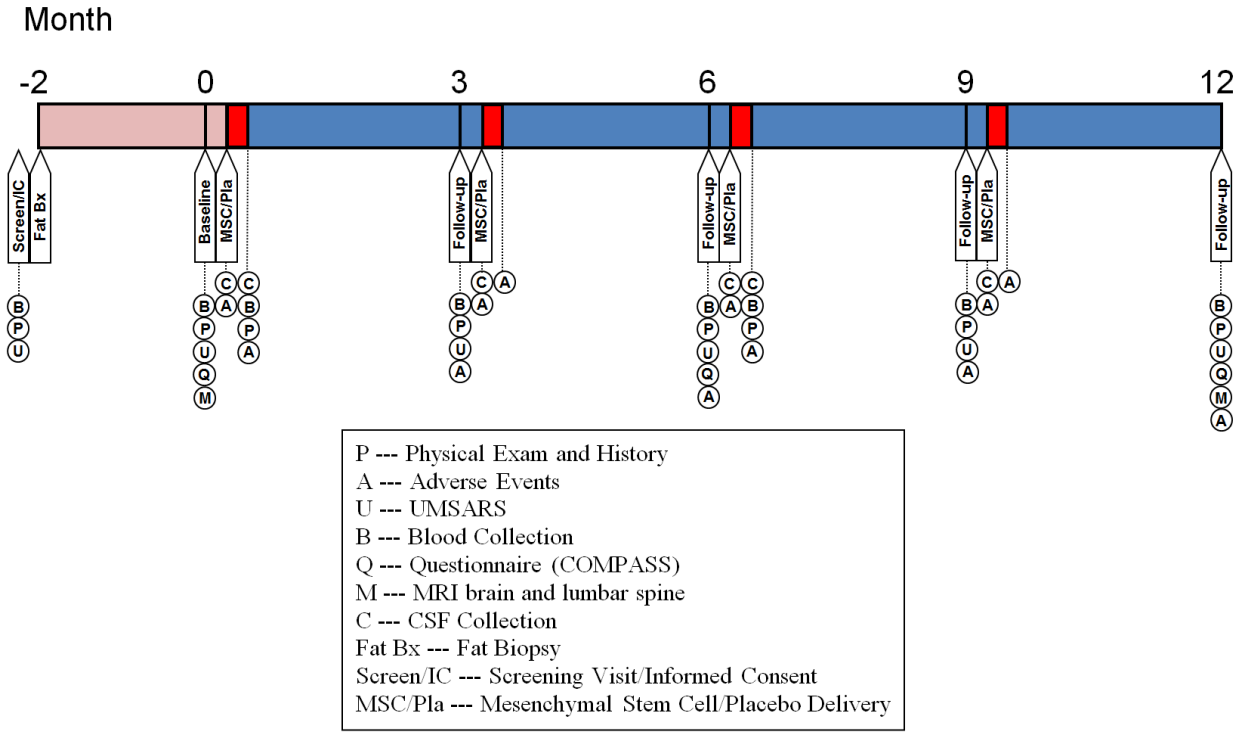
You will meet with the study physician assigned to assess adverse events who will discuss with you any adverse effects you may have experienced as a result of your treatment. Please do not discuss adverse events with the doctors evaluating your MSA and its progression to make sure they remain blinded to your treatment assignment.

The study timeline is summarized as follows:

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**



P --- Physical Exam and History
A --- Adverse Events
U --- UMSARS
B --- Blood Collection
Q --- Questionnaire (COMPASS)
M --- MRI brain and lumbar spine
C --- CSF Collection
Fat Bx --- Fat Biopsy
Screen/IC --- Screening Visit/Informed Consent
MSC/Pla --- Mesenchymal Stem Cell/Placebo Delivery

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

The test schedule is summarized as follows:

[1] A second biopsy will be done within 8 weeks if necessary
[2] Performed by a neurologist not involved in patient scoring
[3] Phone follow-up only (performed by a neurologist not involved in patient scoring)

	Within two weeks of enrollment	Week -8	Week 0	Week 1	Week 13	Week 14	Week 26	Week 27	Week 39	Week 40	Week 52
Eligibility/Consent	X										
Medication review	X		X		X		X		X		X
Review of AEs			X[2]	X[2]	X[2]	X[3]	X[2]	X[2]	X[2]	X[3]	X[2]
Pregnancy test	X										
MOCA	X										
Fat biopsy		X[1]									
Study treatment			X		X		X		X		
Blood draw	X		X	X	X		X	X	X		X
CSF collection			X	X	X		X	X	X		
MRI brain & l-spine			X								X
UMSARS I only	X										
UMSARS I-IV			X		X		X		X		X
Modified UMSARS			X		X		X		X		X
COMPASS select			X				X				X
Medical History	X										
Physician visit	X		X	X[2]	X		X	X[2]	X		X
GME	X		X	X[2]	X		X	X[2]	X		X
Neurologic exam	X		X	X[2]	X		X	X[2]	X		X
Vitals/weight			X	X	X		X	X	X		X

[1] A second and third biopsy will be done if necessary
[2] Performed by a neurologist not involved in patient scoring
[3] Phone follow-up only (performed by a neurologist not involved in patient scoring)

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

We have experience thus far with 30 patients with MSA who have received stem cell injections into the spinal fluid. In those patients, we have seen 18 patients with thickening of nerves on MRI after treatment. Nine of those patients developed low back pain and/or pain in the back of their thighs.

None of those patients had neurologic deficits or abnormal exam findings as a result of this. We believe that this finding has to do with your body's reaction to the study treatment (the stem cells or the injection solution). One patient had imaging evidence of a subdural hematoma (bleeding) in the area of repeated spinal taps. This resolved on its own, did not cause symptoms, and was only discovered on scheduled MRI imaging.

Eight patients noticed mild to moderate temporary headaches following at least one of the lumbar punctures. Two patients experienced a self-limited fever after the first stem cell administration. Some patients had falls, fatigue, urinary tract infections and one patient developed retention of urine, all of which are common occurrences in MSA and likely related to the disease itself and not the study treatment. Temporary cramping of calf muscles and lower extremity muscle twitching was rarely reported, and it is unclear whether these symptoms were related to the study treatment.

The information about the risks of injection of mesenchymal stem cells into the cerebrospinal fluid is still limited and unforeseen adverse effects are possible. Like with any medication, allergic reactions are a possibility.

The risks of drawing blood include pain, bruising, and rarely, infection at the site of the needle stick. For most patients, placement of a saline lock is well tolerated. However, it rarely causes bleeding, bruising, swelling, and possibly infection.

For most patients, spinal tap is well tolerated. However, it may cause pain, headache, bleeding, bruising, swelling and possibly infection at the needle site.

There are no known side effects associated with magnetic resonance imaging (MRI). However, having an MRI may mean some additional discomfort for you. In particular, you may be bothered by feelings of claustrophobia (a "closed in" feeling) and by the loud banging noise during the test. Temporary hearing loss has been reported from this loud noise. That is why we ask you to wear ear plugs. At times during the MRI, you may become uncomfortable due to having to lie completely still, this usually resolves after the scan is completed.

The MR dye (FDA-approved gadolinium) may cause headache, discomfort at the injection site, nausea or vomiting, tingling, dizziness, and/or warmth at the injection site. Approximately two percent (1 out of 50 patients) experience some side effects. However, these are mostly mild such as nausea and headache. Similar to most medications, gadolinium may cause allergic reactions. In rare cases (1 out of 10,000 patients) the allergic reaction can be life-threatening, if untreated. The radiologist and radiology nursing staffs are trained to treat such allergic reactions, should they arise. Gadolinium should be given with caution in patients with a history of seizures, severe kidney disease, asthma, or hemolytic anemia. If you have any of these conditions, please tell your doctor so that you can discuss whether you can safely participate in this study.

Studies have shown that small amounts of gadolinium may remain in the body of patients who have received these injections. The effect of this, if anything, is unknown at this time.

Exposure to gadolinium contrast material in patients with poorly functioning kidneys may result in a rare but serious and potentially fatal condition known as nephrogenic systemic fibrosis (NSF). This progressive disorder can lead to thick, coarse, or hard skin that severely restricts movement of the joints. If you are known to have kidney disease or poor renal function, you may not be able to take part in this part of the study. The investigator may also ask you to give a blood sample to test your creatinine level; this level is used to measure how well your kidneys are working. If your creatinine level is high, you may not be able to take part in this study.

Pregnancy and Birth Control:

1) Will women of child-bearing-potential be allowed to participate in this study?

Yes: Women of child-bearing-potential will be able to participate in this study if they have a negative pregnancy test and agree to use acceptable birth control (see #4) since the risks to an unborn child are either unknown or potentially serious.

2) Do you need to have a pregnancy test done to be part of the study?

Yes: As part of this study a pregnancy test is required for all women who are able to become pregnant. A urine pregnancy test will be performed. You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

3) Will men who are able to father a child be allowed to participate in this study?

Yes: Men who are able to father a child are allowed to take part in this study.

4) What types of birth control are acceptable?
   - Surgical sterilization
   - Approved hormonal contraceptives (such as birth control pills, Depo-Provera) used with a second non-hormonal form of birth control.
   - Barrier methods (such as a condom or diaphragm) used with a spermicide
   - An intrauterine device (IUD)
   - Partner's vasectomy

Risk summary
Many side effects go away shortly after the injection is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death.

Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, we will continue to collect any adverse events that you may have experienced since leaving the study. However, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

This study may not make your health better. However, this study is an important step towards our understanding of the effects of mesenchymal stem cells when injected into the spinal fluid. The information we learn from this study may benefit people with MSA in the future.

What alternative do you have if you choose not to participate in this research study?

You do not have to be in this study to receive treatment for your condition. You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Fat biopsy
- Blood and spinal fluid tests being performed for the study
- Spinal taps
- Outpatient visits as part of this study and inpatient stay at the research unit
- Study treatment (mesenchymal stem cells or placebo)
- MRI of the brain and lumbar spine
- Pregnancy test (if required)

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular clinical care.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will be reimbursed for travel expenses (hotel, car mileage, other ground transport, meals, and airfare) up to $2500. In the event that visits in addition to those outlined in this consent form should become necessary (for example to assess an adverse event or in case of the need for an extra study visit due to problems with the study product), you will be reimbursed for travel expenses related to those extra visits up to $500 per extra visit. However, the total amount of travel reimbursement for the study cannot exceed $4000. In order to receive reimbursement, you must provide a copy of the original receipts for those expenses.

You will also receive $500 if you complete all parts of the study. If you do not complete the study, this amount will be prorated based on the number of visits you completed.

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

There is a very small chance that some commercial value may result from the use of your sample. This could include new products like a drug or a test to diagnose a disease. If that happens, you will not be offered a share in any profits.

Will your information or samples be used for future research?

Unless you give your permission below, your information or samples collected for this study will not be used or shared for future research, even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.
As part of this study, there will be the option of having a sample of your spinal fluid and blood stored for future studies. You can still take part in the main study even if you don't want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research.

Researchers at other institutions may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research may be on any topic. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

If you approve release of your information and/or samples by checking 'yes' below, Mayo may send the information and/or samples to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Some future studies may examine your DNA, the genetic information you inherited from your parents (genetic testing). If there are findings which may be useful for your health care, the researchers may contact Mayo Clinic, so Mayo Clinic can give you the option of learning the results. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed. It is also possible that reidentified information could be used in discriminating ways, and there could be additional unknown risks. We will make every effort to protect your confidentiality.

Please read the following statements and mark your choices:

1. I permit my sample to be stored and used in future research of Drs. Low, Singer, and colleagues at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

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

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Study file information will be stored in locked file cabinets in a secure location that can only be accessed by cardkey access. Access to study files will be limited to the study team only. Data about the cell acquisition, characterization and release criteria will be maintained using standard procedures in the Human Cell Therapy Laboratory.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Plummer Building PL 3-02
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

There is no expiration or end date related to the Sponsor's use of your health information received from Mayo Clinic as part of this study.

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 30, 2025**
Not to be used after: **May 29, 2026**

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature