Official title: Multi-center, randomized, double-blinded assessment of Tecfidera® in extending the time to a first attack in radiologically isolated syndrome (RIS) (ARISE)

NCT number: NCT02739542

IRB Approved date: 12/05/2018

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Multi-center, randomized, double-blinded assessment of Tecfidera in extending the time to a first attack in radiologically isolated syndrome (RIS) (ARISE)
Sponsor:	The University of Texas Southwestern Medical Center
Funding Agency:	Biogen
Study Doctors:	Darin Okuda, MD

You may call the study doctor or research personnel during regular office hours and at other times at 214-645-8800.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to find out whether an FDA-approved drug for relapsing forms of multiple sclerosis (MS) called Tecfidera (dimethyl fumarate) can treat your condition better or more safely than no medication.

Why is this considered research?
This is a research study because, currently, there is no FDA-approved medication for Radiologically Isolated Syndrome (RIS).

The following definitions may help you understand this study:
- Double-blind means neither you nor the researchers will know which study drug you are receiving.
- Placebo-controlled means that some participants will get a placebo. A placebo looks like the investigational drug but it includes no active ingredients.

- Randomization means you will be placed by chance (like a flip of a coin) in one of the study groups.
- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have Radiologically Isolated Syndrome (RIS).

Do I have to take part in this research study?"
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
About 50 people will take part in this study at UT Southwestern Medical Center. This study also is taking place at a number of other medical facilities around the country. There will be a total of 90 people participating in this research study throughout the United States and/or other countries.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Screening Procedures
To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

Procedures and Evaluations during the Research

Screening (approximately 2 hours):
- Review of inclusion and exclusion criteria
- Evaluation of clinical and radiological data

- Consent and Discussion of Study Expectations

Week 0, +/- 2 weeks (approximately 2.5 hours)
- Record Demographics, and Medical and Clinical History
- Physical examination including vital signs
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Pregnancy test – urine
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw (½ tablespoon): Lab tests – CBC & CMP
- Biological mechanistic samples for future use (including DNA and RNA)
    - Serum
    - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla Recommendation for MRI of the cervical spine with and without contrast (per medical standard of care)
- Obtain randomization number
- Administer Study Medication
- Review any adverse events and concomitant medications

Week 4, +/- 2 weeks (approximately 20 minutes)
- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications

Week 8, +/- 2 weeks (approximately 20 minutes)
- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications

Week 12, +/- 2 weeks: (approximately 20 minutes)
- Blood draw (½ tablespoon): Lab tests – CBC & CMP
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications
- Dispense Study Medication

Week 24, +/- 2 weeks: (approximately 20 minutes)
- Blood draw (½ tablespoon): Lab tests – CBC & CMP
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications
- Dispense Study Medication

Week 36, +/- 2 weeks: (approximately 20 minutes)

- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications
- Dispense study medication (via mail or patient pick up)

Week 48, +/- 2 weeks (approximately 1 hour):

- Review of Interval Medical History
- Physician examination (including vital signs)
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP
- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
  - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla (to be performed at UT Southwestern ONLY
- Dispense Study Medication
- Review any adverse events and concomitant medications

Week 60, +/- 2 weeks: (approximately 20 minutes)

- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Assessment of adverse events and changes in medications
- Dispense study medication (via mail or patient pick up)

Week 72, +/- 2 weeks, (approximately 20 minutes):

- Blood draw: (½ tablespoon): Lab tests – CBC & CMP
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Dispense Study Medication
- Review any adverse events and changes in medications

Week 84, +/- 2 weeks: (approximately 20 minutes)

- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Dispense study medication (via mail or patient pick up)
- Review any adverse events and changes in medications

Week 96, +/- 2 weeks (approximately 2 hours):

- Review of Interval Medical History
- Physician examination (including vital signs)
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP
- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
  - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla
- Recommendation for MRI of the cervical spine with and without contrast (per medical standard of care)

Week 108, +/- 2 weeks: (approximately 20 minutes)

- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Review any adverse events and changes in medications
- Dispense Study Medication (via mail or patient pick up)

Week 120, +/- 2 weeks, (approximately 20 minutes):

- Blood draw (½ tablespoon): Lab tests – CBC & CMP
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Dispense Study Medication
- Review any adverse events and changes in medications

Week 132, +/- 2 weeks: (approximately 20 minutes)

- Telephone conversation
- Assessment for medical or medication difficulties
- Assessment of medication compliance
- Review any adverse events and changes in medications
- Dispense Study Medication (via mail or patient pick up)

Week 144, +/- 2 weeks (approximately 2 hours):

- Review of Interval Medical History
- Review of AEs and Concomitant Medications
- Physician examination (including vital signs)
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP

- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
  - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla
- Recommendation for MRI of the cervical spine with and without contrast (per medical standard of care)
- Collect all remaining study medication

Relapse Visit (approximately 2 hours):

- Review of Interval Medical History
- Review any adverse events and changes in medications
- Physician examination (including vital signs)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP
- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
- Recommendation for Standardized brain MRI at 1.5 or 3.0 Tesla at the discretion of the treating neurologist (per medical standard of care)

Unscheduled Visit (approximately 2 hours):

- Review of Interval Medical History
- Review any adverse events and changes in medications
- Physician examination (including vital signs)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- If standard of care brain CBC, CMP obtained at this visit, data should be recorded.
- If standard of care brain and/or cervical spine MRI completed at this visit, data should be recorded.

Early Withdrawal/Discontinuation or End of Study (approximately 2 hours):

- Review of Interval Medical History
- Review any adverse events and changes in medications
- Physician examination (including vital signs)
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP
- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
  - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla
- Recommendation for MRI of the cervical spine with and without contrast (per medical standard of care)
- Collect all remaining study medication

Group Assignment

If the researchers believe you can take part in this study, you will be assigned randomly (like a flip of a coin) to receive either Tecfidera (dimethyl fumarate) or placebo (inactive substance). You have a 1 in 2 chance of receiving Tecfidera (dimethyl fumarate) or placebo.

The group you will be in is decided by a computer-generated program established before the research begins. Neither you nor the researchers will be allowed to choose which group you are assigned to.

Study Medication/Intervention

If you decide to participate in this study you will take either:

- Tecfidera (dimethyl fumarate), 1 capsule (120 milligrams) twice a day for 7 days and then increase to 2 capsules (240 milligrams) twice per day thereafter

  OR
- 1 tablet of placebo (inactive substance) twice a day for 7 days and then increase to 2 capsules twice a day

If you cannot tolerate the study medication by mouth, you may be offered to switch to another study medication called pegylated interferon (Plegridy).

Magnetic Resonance Imaging

You will have magnetic resonance imaging (MRI) of your head. For this procedure, you will lie quietly inside a large, doughnut-shaped magnet for about 45-60 minutes. Your head will rest in a special helmet-like holder to help you keep your head still.

How long can I expect to be in this study?

The study will take place over 144 weeks (approximately three years), or until End of Study (EOS) which is March 31, 2021

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?

Study Procedure/Intervention

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Tecfidera (dimethyl fumarate) may cause some, all or none of the side-effects listed below.

Frequent (>15%)

- Headache

Occasionally (>5%)

- Abdominal pain

- Flushing (redness of the skin that may be accompanied by feeling warm, burning, sweating, or other symptoms)

Rare (<1%)

- Liver or kidney damage

- Diarrhea
- Nausea/Vomiting
- Elevated liver enzymes

Serious but Rare

- Death
- Irregular Heart Beat
- *PML (Progressive multifocal leukoencephalopathy) a rare brain infection that usually leads to death or severe disability

*Progressive multifocal leukoencephalopathy (PML). Some patients receiving Tecfidera (dimethyl fumarate) have developed a very rare but severe viral infection of the brain. There have been no documented cases of PML in patients with RIS. Some patients who were being treated for other indications other than MS developed PML. PML causes brain damage and is usually fatal or leads to severe disability. It occurs almost exclusively in people with severe immune deficiency, such as transplant patients on immunosuppressive medications or patients receiving certain kinds of chemotherapy (drugs to treat cancer).

Symptoms of PML are diverse, progress over days to weeks, and include the following: progressive weakness on one side of the body or clumsiness of limbs; disturbance of vision; and changes in thinking, memory and orientation, leading to confusion and personality changes. The progression of deficits can lead to severe disability or death.

Pegylated Interferon beta-1a (Plegridy):

More common	*Less common*
• Blue-green to black skin discoloration • chills • cough or sore throat • diarrhea • dizziness • extremely high fever or body temperature • fast, shallow breathing • fast, weak heartbeat • fever	• Dark urine • decreased appetite • general feeling of tiredness or weakness • itching skin • light-colored stools • stomach or abdominal pain • yellow eyes or skin

• general feeling of discomfort or illness • joint pain • muscle aches and pains • muscle cramps • pale, clammy skin • runny nose • shivering • sweating • thirst • trouble sleeping • unusual tiredness or weakness • vomiting • Difficulty with moving • itching, rash, redness, soreness, swelling, or warmth at the injection site • lack or loss of strength • muscle stiffness • pain, redness, or sloughing of skin at the injection site	*Rare* • Difficulty with swallowing • hives or welts • large, hive-like swelling on the face, • puffiness or swelling of the eyelids or around the eyes, face, lips, or tongue • redness of the skin • skin rash • tightness in the chest

Magnetic Resonance Imaging (MRI).

There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time

You may also experience some discomfort and fatigue from lying still during imaging.

If you have any metal clips or plates in your body, you should tell the investigator.

MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips

- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

The contrast agent you will receive is FDA-approved and used routinely for MRI exams. It contains a material called Gadolinium (dye solution used to highlight organs or tissues during imaging). The injection of Gadolinium may cause discomfort like headache, nausea, strange taste, or coldness at site of injection. These symptoms occur in less than 1 out of 20 patients receiving Gadolinium and go away quickly. There is a small risk of a severe allergic reaction that can cause breathing difficulties and/or low blood pressure, and these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician and nursing staff will be available to evaluate and, if necessary, provide treatment.

People with severe kidney failure who receive Gadolinium (dye solution used to highlight organs or tissues during imaging) are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF). This disease can cause wide spread tissue scarring or hardening (fibrosis). In rare cases NSF can lead to lung and heart problems and cause death. If you have severe kidney failure and receive gadolinium, the risk of developing NSF is 1-5%. We may perform a blood test 30 days before your MRI to check how well your kidneys are working before you receive the Gadolinium. This test may be repeated closer to your MRI appointment if your medical condition has changed. If your kidneys are working at levels known to be at risk for NSF, you will not receive Gadolinium. You will not receive Gadolinium for research purposes if you have sickle cell disease (a disease of the blood cells) since it may put you at risk of developing hemolysis (breakdown of blood cells).

Psychological Stress

Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Sperm, Embryo, Fetus or Breast-fed Infant

Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

(1) surgical sterilization (vasectomy), or
(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a urine pregnancy test will be done, and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or “tubes tied”),
(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),
(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or
(4) an intrauterine device (IUD).

If you do become pregnant during this study, you **must tell the researchers immediately**.

Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

You will have 4 tablespoons of blood collected because you are in this research study.

Placebo

If you receive a placebo, you will not receive active medication for your health problem. If your problem becomes worse, your participation in the research will stop. If this happens, your study doctor can discuss alternative care with you.

Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

Please notify the study doctor or study staff immediately if you experience any of these or any other side effects during the study. You will be monitored throughout the study in order to minimize risks.

How will risks be minimized or prevented?

Potential risks and discomforts will be minimized to the greatest extent possible by using procedures such as:

- All research personnel will receive appropriate training
- The study will be monitored on regular basis
- Evidence of difficulty or side effects may cause the study doctor to withdraw you from the study
- The study doctor may determine that you will need referral for treatment
- A follow-up visit will be scheduled following the treatment in the study

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Store study materials (capsules or injections) in a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Carry information about Tecfidera or Plegridy in your purse or wallet.
- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important

to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with Radiologically Isolated Syndrome (RIS) in the future. Information gained from this research could lead to better treatment options, as well as knowledge about the conversion from RIS to a definite diagnosis of multiple sclerosis (MS).

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options: to remain untreated for your medical condition or to receive standard medical care without research participation.

Please talk to the researchers or your personal doctor about these options.

Will I be paid if I take part in this research study?
Yes.

You will be given the following, if you take part in this research:

- Parking expenses while on campus for research; and
- If you return for an additional MRI at One-Year (UTSW patients only) you will be paid $50.00 upon completion of the procedure; and
- The following will be provided for patients living greater than 75 miles from UTSW: one night lodging (arrangements made and paid for by UTSW) and mileage reimbursement of .54¢ per mile (as calculated by Google Maps)

How will I be paid?
You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. You will also receive instructions on how use the card. In order

receive study payments, your name, address, date of birth and Social Security Number (SSN) will be collected from you by the research staff. All information will be stored in a secure fashion and will be deleted from the UT Southwestern Greenphire ClinCard system once the study has been completed.

Important Information about Study Payments

1. Your SSN is needed in order to process your payments. Should you decide not to provide your SSN, your study participation payment will decreased at the current IRS tax rate. Study payments are considered taxable income and are reportable to the IRS.
2. An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.
3. Your information will not be shared with any third parties and will be kept completely confidential

This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

If you are an employee of UT Southwestern, your payment will be added to your regular paycheck and income tax will be deducted. You will not receive a ClinCard.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a “hold” on all State payments to you. Such a “hold” could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the “hold.”

You will be reimbursed for your parking expenses. In order to receive reimbursement, you will need to turn in all your receipts to the research coordinator.

Will my insurance provider or I be charged for the costs of any part of this research study?

No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above). However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?

It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas.

You retain your legal rights during your participation in this research

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor is a research investigator in this study. He is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Biogen
- Quintiles, Inc.

- Almac
- Core Clinical Unit
- Central Imaging Unit
- Microbiome Laboratory
- Safety Reviewer
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.

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.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Are there procedures I should follow after stopping participation in this research?
Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Return any unused study materials, including empty containers.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Early Withdrawal/Discontinuation (approximately 2 hours):

- Review of Interval Medical History
- Review any adverse events and changes in medications
- Physician examination (including vital signs)
- Visual System tests (Low Vision Contrast charts, Ocular Coherence Tomography (OCT) (to be performed at UT Southwestern ONLY)
- Cognitive/Functional Assessments (Appendix 1)
- Patient Reported Surveys (Appendix 2)
- Blood draw: CBC, CMP
- Biological mechanistic samples for future use (including DNA/RNA),
  - Serum
  - Spinal fluid (CSF) (optional)
- Standardized brain MRI at 1.5 or 3.0 Tesla
- Recommendation for MRI of the cervical spine with and without contrast (per medical standard of care)
- Collect all remaining study medication

Is there anything else I should know before I decide?
Dr. Okuda and Katy Wright have financial interests in the company funding this study. You should feel free to ask questions about this.

Whom do I call if I have questions or problems?
For questions about the study, contact Darin Okuda, MD at 214-645-8800 during regular business hours and also after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.

_____
Name of Participant (Printed)

_____ _____ _____ AM / PM
Signature of Participant Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time