Providence Brain and Spine Institute
9135 S.W. Barnes Road, Suite 363
Portland, OR 97225
t: 503.216.1055
f: 503.216.1021
www.providence.org/brain

Oregon Neurosciences Program

PROVIDENCE
Brain and
Spine Institute

CONSENT FORM FOR A RESEARCH STUDY

Title: Switching relapsing multiple sclerosis patients treated with natalizumab (Tysabri ®) at risk for progressive multifocal leukoencephalopathy to teriflunomide (Aubagio®): Is this safe and effective? (PH&S IRB # 14-011B)

Principal Investigator: Stanley Cohan, MD

Sponsor: Multiple Sclerosis Center of Northeastern New York

INTRODUCTION AND PURPOSE

You are being asked to participate in a research study. This consent form will explain this study and what you need to do to participate. Make sure you understand what is written, and ask as many questions as needed before you decide to take part. After this study has been explained to you, if you choose to participate, you will be asked to sign this consent form.

You have a relapsing form of multiple sclerosis (MS) and are currently being treated with natalizumab (Tysabri®). Blood tests also indicate that you have been infected with the JC virus (JCV) in the past. Some patients treated with natalizumab develop JCV infections of the brain and develop a very serious, and at times, fatal disease called progressive multifocal leukoencephalopathy (PML). Five of every 1000 patients who have tested positive for JCV infection and have been on natalizumab for 2 or more years developed PML. Because of this risk, doctors are interested in finding alternative therapies for MS patients who are positive for JCV infection who are receiving natalizumab.

Your neurologist has recommended that you stop taking natalizumab and switch to teriflunomide (Aubagio®). Aubagio is a medication approved by the Food and Drug Administration for patients with relapsing forms of MS. It is a tablet taken by mouth once a day. To participate in this study, you or your insurance company must cover the costs associated with Aubagio. Please check with your insurance provider to see what your financial responsibility will be for the costs associated with Aubagio.

The purpose of this study is to determine whether teriflunomide is an effective alternative to natalizumab in patients with relapsing MS who are at risk for developing PML.

The exact way(s) by which teriflunomide treats a patient with relapsing MS is not known. It is known to weaken or damage the function, ability to turn on, and ability to multiply of certain white blood cells or lymphocytes, called T-cells. These T-cells are targeted to attack myelin, an insulating layer that covers parts of your nerve cells and helps electrical signals travel quickly in the central nervous system. To date, no patient receiving teriflunomide has developed PML, but this does not mean that patients receiving teriflunomide are not at risk for it.

About 30 people will take part in this study at Providence. Patients will participate in the study for up to two years.

STUDY PROCEDURES

If you decide to participate in this study, you will be asked to sign this consent document after you have had all of your questions answered to your satisfaction. A breakdown of the procedures at each study visit can be found below. Items marked with an asterisk (*) are being performed for study purposes only and are not part of your standard care.

Visit 1 – Screening

- Review of your medical, surgical and MS-specific disease history, including any medications that you may be taking or have taken recently
- A physical examination
- An Expanded Disability Status Scale (EDSS), which is a numerical rating of your neurological system done by your doctor*
- Assessment of depression (Becks Depression Scale), which is a 21 question questionnaire that will take about 10 minutes to complete*
- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- Collection of blood samples for routine lab work to check organ function and a complete blood count (CBC) that measures the amount of white blood cells, red blood cells and platelets in your blood
- Collection of a blood sample for a pregnancy test if you are a woman able to become pregnant*
- Skin or blood test for tuberculosis
- Your doctor or a member of his staff will confirm that your insurance covers Aubagio®
- Magnetic Resonance Imaging (MRI) of your brain

Visit 2 – Baseline

- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- A physical examination
- Assessments of your MS to include an Expanded Disability Status Scale (EDSS) and a Symbol Digit Modalities Test (SDMT) to measure your ability to understand things*
- Collection of blood samples for liver function testing
- Collection of a urine sample for a pregnancy test if you are a woman able to become pregnant*
- A review of your medications and any adverse events since your last visit
- You will begin taking Aubagio® as prescribed by your doctor. You will be required to save all used packaging and bring all used packaging and unused Aubagio® into each office visit during this study.

Month 1, 2, 3, 4, 5

- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- A physical examination
- Assessments of your MS to include an EDSS*
- Collection of blood samples for liver function testing
- Collection of a urine sample for a pregnancy test if you are women able to become pregnant*
- A review of your medications and any side effects since your last visit
- An MRI (magnetic resonance imaging) of your brain

- **MRIs are done more frequently in the first 6 months of this study than for the standard medical care for your condition.**

- Review of Aubagio® dosing*

Month 6

- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- Assessment of depression (Becks Depression Scale)*
- A physical examination
- Assessments of your MS to include an EDSS and a SDMT*
- Collection of blood samples for chemistry and CBC
- Collection of a urine sample for a pregnancy test if you are a woman able to become pregnant*
- A review of your medications and side effects since your last visit
- An MRI (magnetic resonance imaging) of your brain
- Review of Aubagio® dosing*

Month 9 and 18

- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- A physical examination
- Assessments of your MS to include an EDSS*
- Collection of a urine sample for a pregnancy test if you are a woman able to become pregnant*
- A review of your medications and side effects since your last visit
- Review of Aubagio® dosing*

Month 12, 24 or Early Termination

- Measurement of your weight and vital signs (heart rate, blood pressure and temperature)
- A physical examination
- Assessment of depression (Becks Depression Scale)*
- Assessments of your MS to include an EDSS and SDMT*
- Collection of blood samples for chemistry and CBC
- Collection of a urine sample for a pregnancy test if you are a woman able to become pregnant*
- A review of your medications and side effects since your last visit
- An MRI (magnetic resonance imaging) of your brain
- Review of Aubagio® dosing*

Unscheduled Relapse

Should you experience any symptoms of a MS attack at any time during the study, you must contact your study doctor. You may be asked to return to the study clinic. During this visit, your symptoms will be assessed using the same tests and procedures performed at the main study visits. The study doctor will ensure appropriate treatment of your symptoms and check your vital signs.

POSSIBLE RISKS

Aubagio is an approved medication for patients with relapsing forms of MS. There are risks associated with taking Aubagio. The risks listed below are the same risks that may occur while taking Aubagio outside of this research study. Aubagio® may cause all, some or none of the side effects listed below. In addition, unknown side effects may occur, including possible interaction with other medication you may be taking. Most side effects go away after Aubagio® is stopped; however, some may be serious, permanent, or even cause death. If you have any side effects, report them to your study doctor or the research staff. The listed risks are temporary, unless stated otherwise.

There is a risk of your multiple sclerosis symptoms worsening if you switch from natalizumab to Aubagio®. The likelihood of this happening is not known at this time.

Risks Associated with Aubagio®

Common Side Effects (occurring in 10 or more people out of 100)
Nausea
Diarrhea
Abdominal pain
Runny nose
Flu-like symptoms
Throat pain
Hair thinning or loss
Elevated liver function tests that could indicate liver injury
Numbness or tingling in the skin
Rash or itching skin
Decreased number of white blood cells, which weakens your body's ability to fight infection
Increased blood pressure
Less Common Side Effects (occurring in 1 to 9 people out of 100)
Serious decrease in the number of white blood cells, greatly weakening your body's ability to fight infection
Rare Side Effects (occurring in less than 1 patient out of 100)
Inflammation of the pancreas (pancreatitis) which may cause abdominal pain, nausea and vomiting

Risks of Study Tests

During MRI scanning, you are required to lie on your back inside the scanner in a tight space. This may cause discomfort or anxiety. If you are pregnant, you cannot have an MRI scan because the chemical injected, gadolinium, could injure your unborn child.

If you have a metal heart valve, cardiac pace maker, in-dwelling pump, metal fragments in your eyes, or other pins or metal objects in your body, you could be harmed by the MRI scan.

Pregnancy/New Father Warning

If you are pregnant or breastfeeding, you cannot take part in this study. The risks of the study treatment to an unborn baby or nursing child are not known and may cause harm. Woman able to become pregnant will be required to have a urine pregnancy test before starting Aubagio®. If you are a woman able to become pregnant, you will be asked to confirm that, to the best of your

knowledge, you are not pregnant and that you do not intend to become pregnant during your participation in this study.

If you are sexually active, you must take adequate precautions to avoid the possibility of becoming pregnant or fathering a child while in this study. You must discuss these precautions with your study doctor before agreeing to take part in this study.

If you are a male using Aubagio®, you must take adequate precautions to prevent your semen from entering your sexual partner. Aubagio® may be transmitted to your partner through semen.

If you are female and decide to become pregnant, you must stop taking Aubagio®. You should inform your study doctor of this decision right away. It is important that you undergo an 11 day treatment with a medication, called cholestyramine to remove the Aubagio® from your body. It is also important that you continue to take adequate precautions to avoid pregnancy until your study doctor has determined, by means of a special blood test, that the Aubagio® level in your body has been sufficiently reduced. It may be necessary to take a second course of oral cholestyramine, if the first course has not adequately reduced the amount of Aubagio® in your body.

If you become pregnant while using Aubagio®, stop using Aubagio® immediately and contact your study doctor. You will then be treated with an 11 day course of cholestyramine, as noted above. Your study doctor will keep in touch with you until the end of the pregnancy and will ask about the outcome of the pregnancy and the health of your baby. This information will be shared with the study sponsor.

After you complete this study treatment, check with your study doctor to see when it might be safe to breastfeed, become pregnant or become a new father.

Risks Associated with Cholestyramine to Remove Aubagio®

Common Side Effects (occurring in 10 or more people out of 100)
Constipation
Heartburn
Nausea
Vomiting
Stomach ache or pain
Less Common Side Effects (occurring in 1 to 9 people out of 100)
Abdominal bloating or gas
Upset stomach
Fatty diarrhea
Stomach ulcer
Malabsorption syndrome, which is when something prevents your intestines from absorbing important nutrients and fluids
Bleeding in the stomach or intestines, which can cause dark or bloody stool
Pancreatitis (inflammation of the pancreas) that can cause pain, nausea and vomiting
Gall stones (stones in the gallbladder) which can cause pain, nausea and vomiting
Dizziness
Headache

Increased blood sugar, which doesn't usually cause any symptoms
Muscle Cramps

POSSIBLE BENEFITS

You may or may not benefit from taking part in this study. There is no guarantee that you will benefit from taking part in this study. The information obtained from your participation in this study will provide information that may assist others with MS in the future.

OTHER OPTIONS

You may choose not to take part in this study. Your doctor can prescribe Aubagio to you even if you choose not to take part in this study.

GENERAL INFORMATION

Your taking part in this study is voluntary. Your refusal to take part will not affect the health care benefits you have. If you decide to take part, you are free to stop at any time without any effect on your medical care, your relationship with your doctor(s) or Providence Health & Services.

If you leave the study, you may be asked to take tests to monitor your safety.
While in this study, any important new information that may affect your wish to continue taking part will be given to you.

Your study doctor may remove you from this study at any time if he/she thinks it is medically necessary, you have a serious side effect, you do not follow the study plan, or if the study is cancelled.

COSTS

You are responsible and must pay for the costs of your routine medical care and medications (such as the costs associated with Aubagio®); however, these costs may be covered, at least in part, by most major insurance companies or Medicare.

The study sponsor will pay for all neurology study visits, as well as for all of the tests that are ordered as part of your participation in this study, such as pregnancy tests (if needed) and the additional MRIs performed for the study only and not considered standard care. The study doctor and the research coordinator will be responsible for making sure these tests are billed to this study, and not you or your insurance company.

Your study doctor is being paid by the sponsor to take part in this study. This is to pay for tests and to conduct this study.

You will be compensated for your time and travel associated costs related to your participation in this study. You will receive $50.00 for each completed study visit. You will receive up to a maximum amount of $600.00 if you complete all study visits as scheduled. If you do not complete the study, for any reason, you will still be paid for each study visit you do complete. Payments are issued quarterly, which is about every three months, and come in the form of a check that is sent to the home address that you have given the study team.

LIABILITY

If you are injured as a result of taking part in this study, all of the necessary medical facilities are available for treatment, as is reasonably possible.

Compensation from the sponsor will not be provided in the event of any research-related injuries.

Providence Health & Services is not the sponsor of this research and is not able to offer you financial payment, nor to pay for the costs of medical treatment should you be injured as a result of taking part in this research.

You do not give up any of your legal rights by signing this consent form and taking part in this study.

PRIVACY

Your medical and study records are personal and private and only your study doctor, yourself and anyone you allow have the right to look at your records. It is important that the research staff, the FDA, the Center for Medicare and Medicaid Services (CMS), the Providence Health & Services Institutional Review Board (IRB – a committee that reviewed this research to protect your rights), and representatives of the Multiple Sclerosis Center of Northeastern New York be able to look at your medical and study records. When you sign this consent form, you agree to allow this. If results of this study are reported in medical journals or at meetings, your identity will remain secret.

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) gives you certain rights to protect the privacy of your medical information and records. Under HIPAA, you must give your permission before anyone uses or shares your medical information. This information is also called protected health information (PHI). Your rights, as well as the reasons for using your PHI, are described below.

The sponsor and your study doctor(s) will need to use your PHI for this study. Your study doctor will record PHI about you on study forms that are given to the sponsor. This includes your name, address, telephone number, date of birth, past medical records and the results of tests and procedures done during this study. The part of your personal health information sent by your study doctor to the sponsor usually does not identify you personally (for example, by name, address, or social security number.) Instead, the study doctor uses your date of birth, initials, and a code dumber on the study data sent to the sponsor.

By signing this consent form, you agree to allow your study doctor and the research staff to use and share your PHI for the following reasons:

- Make decisions about your medical care
- Evaluate the results of this study

- Make conclusions about the study results
- Provide study results to other study doctors
- Re-evaluate study results in the future, as needed
- Include your study information with results from other similar studies
- Send study information to government health agencies; this may also include government agencies in other countries
- Report side effects to the FDA and other government agencies
- Send study information to representatives of the study sponsor
- Any other purposes as described in this consent form.

If you are not willing to allow your PHI to be shared, you will not be able to take part in this study.

The study sponsor and their representatives, the IRB and any regulatory agencies may review your medical records and make copies. The reasons this might happen are to make sure this study is being done properly, study information is being collected correctly, and for other purposes allowed by law.

Once your PHI is shared with others, it is no longer protected by HIPAA law. However, it will be kept as confidential as possible.

Your permission to use and share your PHI will not end unless you change your mind. You may cancel your permission at any time by sending a written notice to your study doctor. Your PHI for this study will no longer be used or shared. In some circumstances, your study doctor will need to use or share your PHI to continue this research study.

If you cancel your permission, you will no longer be able to take part in this study. The sponsor will still use any PHI they received before you cancel your permission.

If you have questions about your privacy rights, please call the Providence Health & Services HIPAA Privacy Officer at (503) 574-9123.

QUESTIONS:

Any questions you have about this research study or a research-related injury can be answered by:

Study Doctor: _____

Research Coordinator: _____

Any questions you have about your rights as a research subject will be answered by the Providence Health & Services Institutional Review Board at (503) 215-2046.

You are free to ask questions about this study at any time.

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.

CONSENT:

I have read all of the above, asked questions and received satisfactory answers about what I did not understand. I agree to take part in this research study. I will be given a signed copy of this consent form for my records.

_____
Name of Patient (Please Print)

_____
Signature of Patient Date

_____
Name of Person Obtaining Consent (Please Print)

_____
Signature of Person Obtaining Consent Date