

**Inside: Important news
for tuberous sclerosis
complex (TSC) patients
with subependymal giant
cell astrocytomas (SEGA)**



EXIST-1

EXamining everolimus In a Study of TSC

*This is an investigational study; there is no guarantee
that everolimus will become commercially available
for this indication.*

New Clinical Research Study for TSC Patients with SEGA

What is a clinical study?

Clinical studies (also called medical research) are investigations that help doctors to find new therapies or new ways of using existing therapies that may improve the treatment of diseases. All new medications undergo a thorough review process, which includes clinical studies, before an authority allows them to become available to the general public. In the United States, this authority is the Food and Drug Administration (FDA), and in Europe, it is the European Medicines Agency (EMA). During a study, researchers follow a strict set of procedures and guidelines approved by the FDA and/or EMA. As a study progresses, researchers are required to report results of the study to the government agencies that monitor and protect the study participants.

What is the name of the clinical study for SEGA patients?

A pharmaceutical company named Novartis Pharmaceuticals Corporation is sponsoring a large clinical study, named EXIST-1, for TSC patients with SEGA. EXIST-1 stands for **EX**amining everolimus **I**n a **S**tudy of **T**SC. The goal of this clinical study is to learn whether a new drug, everolimus, will be beneficial for TSC patients with SEGA.

What is everolimus (RAD001)?

Everolimus (also known as RAD001) is being studied as a treatment for patients with various other types of cancer, either alone or in combination with other cancer treatments. Everolimus (RAD001) stops cancer cells from making new cancer cells and also cuts off the blood supply to the cancer. This may slow the growth and spread of SEGA in people with TSC.

Who can participate in the EXIST-1 study?

You may be eligible to participate in this study if you have been diagnosed with TSC-associated SEGA and have test results showing either a series of growths, a new SEGA lesion at least 1.0 cm in diameter, or new or worsening fluid around your brain.

There are other important requirements that your doctor can review with you, should you be interested in participating in this study.

What is the time commitment for patients in this study?

This study does not have a set treatment time frame. If you join the EXIST-1 study, clinic visits will occur every 2 weeks during the first 2 months, then every 4 to 6 weeks until week 24 of the study, after which point, visits will occur every 12 weeks until study completion. You may continue to take the study drug until the disease gets worse, until you decide to no longer take part in the study, until your doctor decides that it is in your best interest to stop treatment, or until the end of the extension phase of the study (3 years after the last patient is entered into the study), whichever comes first.

How will my progress be tracked?

While you are participating in this study, highly trained doctors and nurses will monitor you closely, using a visit evaluation schedule. At each clinic visit, you will be asked questions about your medical history and about any medications you are currently taking or have taken in the past. Also at each clinic visit, you will have tests that evaluate

how well you are breathing and the condition of your lungs. At some of the visits, you will have a complete physical exam as well as an exam of your nervous system. Your vital signs will be taken, and you will be asked about your ability to perform every day activities.

A magnetic resonance image (MRI) of the brain will be taken at months 3 and 6, and then every 6 months after that. Your doctor will take a 24-hour record of the electrical activity of your brain (EEG) at the screening and 6 months later, and take digital photos of any skin lesions you have at the screening, on the first day of treatment, 18 weeks later, and every 3 months thereafter.

If you decide to participate in the EXIST-1 study, it is important to follow all instructions given by your doctor during the entire study period. You will be expected to attend all scheduled office visits, to take your medication exactly as directed, and to report any side effects you may experience. This will enable your doctor to track your progress every step of the way through the different exams and tests. He or she will keep you informed of how the medication is working. Feel free to ask your doctor any questions you may have.

What can I expect while participating in the study?

While participating in this clinical study, you may be at risk for side effects. As with any medication, side effects may vary from person to person.

The most common possible side effects of the study drug everolimus are skin changes (rash) including redness, itching, or irritation; mouth lining changes (stomatitis) revealed through pain, redness, irritation, and swelling in the mouth or mouth ulcers; fatigue; nausea; decrease

of appetite (anorexia); headache; vomiting; diarrhea; constipation; abdominal swelling; and, occasionally, infections. There could be a decrease in the number of your red blood cells, white blood cells, and platelets, as well as lowered levels of some electrolytes (potassium, sodium, calcium, magnesium, or phosphate) in your blood. The levels of glucose, lipids (triglycerides and cholesterol), or liver enzymes (transaminases) in your blood could also increase.

Many side effects go away shortly after everolimus is stopped, but in some cases, side effects may be serious and/or long-lasting. Remember to report any side effects to your doctor or nurse.

In addition, noninfectious pneumonitis, a condition that can cause breathing problems, has been reported in some patients taking everolimus. Frequently, pneumonitis resolves once you stop taking the medication. Your doctor will check for this condition often. You should contact your doctor immediately if you experience sudden, unusual symptoms, such as shortness of breath, coughing, or fever.

Who will pay for the treatment?

Your health insurance will continue to cover your standard health care needs. All study-related costs (study medication, tests, etc) that go above and beyond the standard of care will be paid for by Novartis.

Why should I participate in the EXIST-1 study?

During the EXIST-1 study, patients will gain access to everolimus, a new research treatment, before it is widely available, in addition to continuous medical care at local health care facilities. Active

participants will also be contributing to research of TSC with SEGA that may help other patients in the future.

Treatment in this clinical study may slow or prevent the growth of your SEGA lesions. However, you must also be aware that participation in this study may not benefit you directly.

What is informed consent?

Informed consent is the process of learning the key facts about a clinical study before deciding whether or not to participate. This process continues throughout the study as participants are provided with additional information that may become available.

If you decide to participate in the EXIST-1 study, you will be given an informed consent document to sign. This information will further explain the purpose of the study and what may occur during the study.

What are my rights as a patient in a clinical study?

Study participation is voluntary. The informed consent document is not a contract. If you so decide, you are free to withdraw from the study at any time, or you may be withdrawn by your doctor if he or she feels that it is in your best interest to do so.

Please ask your doctor or nurse for more information about your rights as a clinical study participant.

How can I enroll in this study?

For further information or to enroll in this clinical study, please talk to your doctor.

How can I learn more?

For more information about EXIST-1 and everolimus, please visit www.novartisclinicaltrials.com or call the Novartis Clinical Trials Hotline at 1-800-340-6843 (US only).

For other information, please visit these independent organization and government Web sites.

Novartis Pharmaceuticals Corporation

www.novartisclinicaltrials.com

Tuberous Sclerosis Alliance

www.tsalliance.org

National Cancer Institute

cis.nci.nih.gov

National Brain Tumor Foundation

www.brainumor.org

American Brain Tumor Association

www.abta.org

The Childhood Brain Tumor Foundation

www.childhoodbraintumor.org

Pediatric Brain Tumor Foundation of the United States

www.pbtfus.org

**Thank you for taking the time to learn
about the EXIST-1 study.**

**Ask your health care professional for
more information.**

Doctor Contact Information

Name:

Address:

Phone:

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Reference: Data on file. Novartis, 2009.

