

Sirolimus Research Study for Cognitive Impairments in Sturge-Weber syndrome (IRB00079722)

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This research will study the safety of sirolimus for the treatment of cognitive impairments in Sturge-Weber syndrome (SWS) brain involvement. Ten people will join this study. Only study drug will be given. There will not be placebo. You will still take your current medications while in this study. The impact of sirolimus on cognitive impairments will be studied. We will use these results to plan a larger trial in the future.

Sirolimus has been studied clinically in cognitive impairments and seizures in tuberous sclerosis. Sirolimus has also been used in small clinical studies of vascular malformations.

Sirolimus helps block a pathway known for boosting cell growth. This pathway is turned on in blood vessel malformations in SWS. This pathway involves the single genetic change that is the source of SWS. This pathway could be the beginning of a future treatment option.

Low Dose Sirolimus Side Effects:

This drug trial will use low-dose sirolimus. Low-dose sirolimus has been dealt with well in clinical studies. The below side effects are for doses much higher than the dose used for this study. The below side effects are NOT expected with the low dose for this study.

Common side effects:

Heart: swelling, high blood pressure, swelling in feet or legs

Skin: acne, rash

Hormones: high blood cholesterol

Digestive Track: abdominal pain, constipation, diarrhea, nausea

Blood: low blood platelet count

Muscle and Skeleton: joint pain

Neurologic: headache

Kidneys: increase of waste in the blood, urinary tract infectious disease

Lungs: nose bleed

Other: fever, pain

Rare, but serious side effects:

Heart: blood clot inside the heart

Skin: cancers of the skin

Hormones: high lipid levels, high blood levels of fats

Digestive Track: inflammation of the pancreas

Blood: blood clots, fluid cysts, low blood cell counts, blood clotting disorder

Liver: clotting of the liver artery, toxicity of the liver

Immune System: kidney disease, BK virus associated (virus associated with liver transplant), cancer of the lymphatic system, abnormal growth of lymph nodes, mycobacteriosis (bacterial disease), sepsis (whole-body reaction to an infection), cytomegalovirus (rare infection), Epstein-Barr virus (a type of herpesvirus)

Neurologic: progressive multifocal leukoencephalopathy (disease of the white matter in the brain)

Kidneys: hemolytic uremic syndrome (syndrome associated with destruction of the blood cells), nephrotic syndrome (excessive protein in the urine)

Lungs: bronchial anastomotic dehiscence (airway complications associated with lung transplant surgery), scarring of the lung tissue, inflammation of the lung tissue, blood clots inside the lungs, bleeding from the lungs

Blood draw side effects: During blood draws, you may experience some discomfort, bruising, or transient pain at the site of needle entry into the vein. There is a remote risk of fainting. Infection could occur at the place where the needle goes into the arm. We will use a sterile technique to help prevent infection.

EEG side effects: There is minimal risk associated with routine EEGs, especially since we are not using sedation. Skilled clinical technicians will perform the EEG. There is a chance you may become restless or agitated during the procedure. However, the use of age-appropriate DVDs, sound recordings, and presence of friends/family may help to minimize restlessness or agitation.

The medical risks associated with joining the study, are believed to be similar to continuing clinical care. All medications used to treat seizures in Sturge-Weber syndrome have associated risks and side effects.

There is the risk of loss of confidentiality in allowing us to see your medical information. We will do our best to keep your personal medical information private. All information from this project will be kept in a locked cabinet and on a secure computer at the Kennedy Krieger Institute.

If you ask to have your photographs destroyed at the end of the study, we will digitally delete all electronic files. We will also shred all hard copies. This information will remain separate from your medical record. All members of the research team have been trained in confidentiality law and methods. Further, should the information we obtain from this study become part of a published report, this report will not identify you as a participant in this study.

You may get tired or bored when we are asking you questions. You may find it tiring or boring if you are asked to complete questionnaires. You do not have to answer any question you do not want to answer.

Participation in the study involves a significant time commitment. This time is not part of routine clinical care.

There may be side effects and discomforts that are not yet known.

To join this study, you (or your child) must:

- 1) Have Sturge-Weber syndrome brain involvement as defined on neuroimaging
- 2) Be between the ages of 3 years and 31 years-old
- 3) Be on stable seizure medications
- 4) Be able to come to all clinic visits (at least 6 clinic visits over the next 6 months)
- 5) Have required blood work done (at least 6 blood draws over the next 6 months)
- 6) Be willing to sign written consent
- 7) Report immediately to Dr. Comi (or Dr. Hammill) with any side effects or concerns

This study is supported by the Faneca 66 Foundation, the National Institute of Health, and Pfizer Pharmaceuticals (study drug only). If you want to join the study or learn more, please contact the study Principal Investigator, Dr. Comi, at 443-923-9127 or comi@kennedykrieger.org. You can also contact the co- Principal Investigator, Dr. Hammill, from Cincinnati Children's Hospital Medical Center at adrienne.hammill@cchmc.org.