Study Title:	Janus Kinase Inhibitor (Baricitinib) for Aicardi Goutières Syndrome
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The Children's Hospital of Philadelphia®

Informed Consent Form and HIPAA Authorization

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Version Date:	May 2, 2023	
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Emergency Contact:	Adeline Vanderver, MD	Telephone: (215) 590-1000 *ask for the Neurology attending on call. They will be able to page Dr. Vanderver.

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Study Overview

You are being asked to take part in this research study because you have medical problems from Aicardi Goutières Syndrome (AGS), and other treatments have not helped.

The purpose of this research study is to test the safety and effect of an investigational drug called "baricitinib". "Investigational" means that it has not been approved by the FDA for use in AGS or in children. On June 1, 2018, the FDA approved baricitinib for treatment of moderate to severe rheumatoid arthritis in adults, severe alopecia areata (sudden hair loss) and COVID-19 in adults.

If you agree to take part, you will be in this research study for about 5 and a half years. If commercial supply is not available by the end of the research study, and if you agree to continue, you may take part in the study for a longer time.

There are differences between this study and your usual care. As a participant in the research you will:

- Receive a study drug.
- Complete study diaries (optional after two years of treatment, but strongly encouraged).
- Undergo regular blood and urine tests.
- Undergo regular physical assessments during research assessments, which may be in addition to regular clinical care.
- Undergo research evaluations by occupational and physical therapists, and research cognitive evaluations.

If you were previously enrolled in the Compassionate Use Treatment Protocol I4V-MC-JAGA (JAGA Compassionate Use study), screening procedures and visits that were already completed as part of the JAGA Compassionate Use study will not be repeated for the purposes of this research study.

The main risks of this study are from the study drug, baricitinib. These include: infection, as the study drug affects affects the immune system. These infections could lead to hospitalizations or death. Some cancers, such as lymphoma, were reported in adults who took the study drug. Some adults also had blood clots in their legs or lungs. Baricitinib can also cause abnormal blood test results.

You may benefit if baricitinib reduces symptoms related to AGS.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this research study if you do not want to. If you take part, you can leave the research study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor.

Please see below for additional details about the study.

How many people will take part?

As many as 50 people may receive baricitinib through this research study.

What is the current standard of treatment for this disease?

There is no current standard of treatment for this disease. The other options available are explained in "What choices do you have other than this research study?" section.

What are the research study procedures?

The research study consists of two periods: the screening period and the study period. In the screening period, you will have a medical exam and will maintain a daily diary. You will also undergo several blood tests and evaluations by physical therapists, occupational therapists, and psychologists. If you are eligible for the main study, you will receive the study drug, baricitinib.

The following tests and procedures are being done in this research study. If a test is or was done as part of your clinical care, we will try to collect the test results from your medical records first. Some of your clinical care procedures may be done more frequently if you participate in this research study.

If you were previously enrolled in the JAGA Compassionate Use study, you will not need to repeat screening procedures and visits that were already completed.

Physical Examination and Vital signs: Exams will be conducted before and during the study. The exam will include measurements of weight, height, blood pressure, pulse, a skin exam, and may include an eye examination.

Study Medication: You will need to take baricitinib by mouth as directed by the research study doctor. How many pills you take will depend on your dose. Doses may be dissolved in liquid and/or administered by mouth or via clinically placed gastrostomy or nasogastric tube.

The dose of baricitinib may be changed several times to determine the dose that works best. This is called “dose adjustment” or “dose escalation”. These could happen at any time during the research study.

At any visit, if the study drug is not helping you, or if it appears to be hurting you, the research study doctor may reduce the dose, ask you to stop taking it for a period of time, or ask you to stop taking it completely.

At every visit, return any unused research study medication and the empty packaging.

Medical Record Review: We will review your medical records throughout the study to collect information about your medical history, current health, diagnosis, treatments, medications, and results of clinical tests.

Diary Scores: You will be asked to fill in a daily diary to assess the signs and symptoms, either on paper or electronically. Filling out the diaries becomes optional after two years of treatment but is strongly encouraged.

Neurologic Function Testing: We will test your movements, speech, balance, alertness, and coordination.

Drug interactions: A team member will take your medical history, along with a listing of any medications you are taking.

Urine tests: You will urinate into a cup or provide a collected urine sample. You can do this in a bathroom without anyone watching you. From your urine, we will measure protein, sugars, blood, and kidney function and look for signs of infection.

Blood Tests: We need to collect blood to measure (blood chemistries, blood counts, etc.). Depending on the study visit, we will collect between 1 and 4 teaspoons of blood. We will do our best to collect the samples at the same time as your routine blood tests, and we will try not to stick you more than once. Blood tests may also include hepatitis and tuberculosis testing if not already done for usual care.

IV Catheter Placement: An IV catheter may be placed at certain visits so that blood can be collected without multiple needle sticks on the same day.

Pharmacokinetic (PK) Testing: Pharmacokinetics is a type of testing that determines how much of a drug is in the blood. This shows us how well the body takes drug into the blood, delivers drug through the blood, breaks down or processes the drug, and removes it.

IFN Signaling Gene Score: Thousands of genes are found in every cell in your body. Each of these genes contains a set of instructions that are read by the cell. This allows your body to make proteins. Some of these proteins respond to interferon and doctors can measure this response by measuring the genes that code for them in the blood. Typically in AGS, the body has abnormally high amounts interferons (IFN). We are testing ways to measure IFN levels, one of which is the IFN signaling gene score. Because this test has not been approved by the FDA, we cannot share the results with you.

Samples for Future Research: During the study, we will collect blood and urine samples from you. By agreeing to participate in the study, you agree to give these samples to CHOP for research purposes.

Pregnancy Test: If you have already started having periods, you will be asked to take a pregnancy test before starting this research study. The results will be shared with your parent(s) or legally authorized representative. If you are found to be pregnant, you will no longer be able to continue taking the study drug. We will ask for your permission to continue reviewing your medical records in order to obtain information on your pregnancy and birth outcomes. You will sign a separate consent form. About 1 teaspoon of blood will be needed for the first test.

After the first test, we will continue to check for pregnancies using a urine sample. This will require that you pee into a cup.

Ionizing Radiation/X-ray: You will have a chest x-ray in order to take pictures of your heart and lungs. You will also have an x-ray of your hand/wrist/fingers (not after a bone age that demonstrates complete growth).

Echocardiogram (Echo): An Echo uses sound waves to create a moving picture of your heart. It can find problems with heart function. You will lie on a padded table or a bed. A technician will glide a special device called a transducer across your chest to take pictures of your heart. A small amount of clear gel will be applied to your chest to help the transducer work better.

Electrocardiogram (ECG or EKG): An ECG is a test that measures the electrical activity of the heart. It is used to examine the heart's rhythm to see if it is steady or irregular. It can also help tell how well the heart pumps blood. Several small pads will be attached to your chest, shoulders and legs. They are attached to a machine that traces your heart activity. This procedure will be completed every other year.

HIV testing: The screening blood tests may include a test for HIV. A counselor will explain the testing and the meaning of the possible results. We will inform you of your test results. Your results will be disclosed to the sponsor in a way that does not identify you by name (you will be identified only by your study ID number). This test will not be repeated if it has already been done for usual care.

Visit Schedule

Study Visit	Time Between Visits	Approx. Visit Length	Procedures/Activities
Visit 1 Required Onsite Visit		3-4 hours	• Obtain informed consent • Medical history/interviews/daily diary • Neurologic function testing • Physical exam/vital signs • Urine and blood tests • Pregnancy blood test (if you are a woman of childbearing potential)

			• Some tests, if not done recently for clinical purposes including a chest x-ray, cardiac evaluation, and blood tests for infections, may need to be performed during this visit.
Visit 2 Onsite Visit	Up to 28 days after Visit 1	4-6 days (several clinic visits during initial dose adjustment may be necessary)	• Confirm eligibility • Medical history/interviews/daily diary • Physical exam/vital signs • Blood and urine tests • Hand/wrist/fingers x-rays* • Receive baricitinib • IV catheter placement and PK testing If dose adjustments occur during these days, you may need to stay at the hospital for up to 12 hours.
Visits 204, 210, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231 Required (onsite)	Visits are every 6 months	2-3 hours	• Interviews/daily diary • Physical exam/vital signs • Functional neurologic assessments every 6 months • Blood and urine tests • Hand/wrist/fingers x-rays (6 months, 12 months, and every 12 months)* • Receive baricitinib • IV catheter placement and PK testing Dose adjustment visits can last up to 12 hours. When functional neurologic assessments are scheduled, the visit may take 1-3 days.
Visits 4, 201, 207, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230 Required (onsite or telephone)	Visits every 6 months, starting at month 3	1-2 hours	• Physical exam/vital signs/daily diary • Blood and urine tests • Receive baricitinib • IV catheter placement and PK testing These visits may be done at CHOP or on the telephone. If done by telephone, you will have blood/urine collected at your local doctor's office or laboratory. Your home doctor will send the lab testing results to the research study doctors at the Investigator Site. With onsite visits including dose adjustments, visits can last up to 12 hours.
Visits 3, 5, 202, 203, 205, 206, 208, 209, 211 (Optional)	*Optional* Starting 2 weeks after Visit 2 (if done)	2-3 hours (if done)	• Physical exam/vital signs/daily diary • Blood and urine tests • Receive baricitinib • IV catheter placement and PK testing These visits may be done at CHOP or on the telephone. If done by telephone, you will have blood/urine collected at your local doctor's office or laboratory.

We will tell you if you need to attend one or more of the optional visits.			Your home doctor will send the lab testing results to the research study doctors at the Investigator Site. With onsite visits including dose adjustments, visits can last up to 12 hours.
Visits 212A, 213A, 214A, 215A, 216A, 217A, 218A, 219A, 220A, 221A, 222A, 223A, 224A, 225A, 226A, 227A, 228A, 229A, 230A Optional We will let you know if you need to attend one or more of the optional visits.	*Optional* Starting after Visit 212 (if done) to allow you to re-align with the in-person versus phone visits schedule, in cases where this schedule would be disrupted	2-3 hours (if done)	• Physical exam/vital signs/daily diary • Blood and urine tests • Receive baricitinib • IV catheter placement and PK testing These visits may be done at CHOP or on the telephone. If done by telephone, you will have blood/urine collected at your local doctor's office or laboratory. Your home doctor will send the lab testing results to the research study doctors at the Investigator Site. • With onsite visits including dose adjustments, visits can last up to 12 hours.
Early Termination visit Required (onsite or telephone)	*Last visit if early withdrawal from the study*	2-3 hours	• Physical exam/vital signs • Blood and urine tests (optional) • IV catheter placement and PK testing (optional)
Visit 801 Optional (onsite or telephone)	28 days after last dose of Study medication	2-3 hours (if done)	• Physical exam/vital signs • Blood and urine tests (optional)

* not after a bone age demonstrating complete growth

If you decide to continue the study because commercial supply is not available, your study schedule will continue as the one described above, with visits every three months, alternating on-site and phone assessments.

You can refer to the study timeline at the end of this consent for a specific explanation about study progression and the study visit numbers over time.

What will be done with my data and specimens during this study?

During the study, we will collect blood and urine samples from you. By agreeing to participate in the study, you agree to give these samples to CHOP for research purposes. If you have previously participated in the JAGA Compassionate Use Study, we will use the data from that study for this study as well.

Will I receive any results from the tests done as part of this study?

Results that could be important for your clinical care will be shared with you. We will not share other results with you.

What are the risks of this research study?

Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your research study doctor or your regular doctor.

While in this research study, you are at risk for the following side effects:

Risks associated with Baricitinib:

Baricitinib is a molecule that blocks the effects of Janus kinases, which are proteins that control your immune system. Drugs that affect the immune system can increase the risk of infection and cancer. Baricitinib may also increase these risks, and others as described below:

Infections

Baricitinib changes the body's ability to respond to infections. It lowers white blood cell counts, including neutrophils and lymphocytes.

Upper respiratory tract infections include symptoms similar to the common cold (cough, stuffy or runny nose, scratchy or sore throat, sneezing). These have been very common in people taking baricitinib. Other infections that were common include shingles and cold sores. Some people with atopic dermatitis had other rashes caused by the cold sore virus.

Serious infections requiring hospitalization were common in people taking baricitinib. These were common during studies.

Unusual infections can occur in people with weakened immune systems. These infections, including tuberculosis, invasive fungal infections, and some viruses, were uncommonly reported in people taking baricitinib. There was one patient with lupus who took either baricitinib or placebo in a clinical trial, and developed shingles and inflammation of the spinal cord at the same time.

Your doctor will decide what treatment, if any, you may need for an infection.

When someone is infected by a virus, the virus may remain inside that person even after all of his or her symptoms have gone away. This is called a latent virus. Sometimes, a latent virus can get reactivated within a person and make him or her sick again. This is called viral reactivation. While taking baricitinib, some people have experienced viral reactivation. If you develop an active viral infection that is at risk of causing harm, we will consider stopping or decreasing study drug until your symptoms have improved.

Subjects who are enrolled in this study and receive the study drug have weakened immune systems, and this may happen more often than in the populations for who baricitinib has been FDA approved (adults with moderate to severe rheumatoid arthritis). This may place them at greater risk of infection.

Subjects with cytopenia (a condition in which there is a lower-than-normal number of blood cells, including red blood cells, white blood cells and platelets) are allowed to be enrolled in this study. Thus, the risk of severe or life-threatening infections is potentially higher than in other populations and some subjects will need prophylaxis (medication or treatment used to prevent a disease from occurring) for certain infections.

If you develop an infection while on baricitinib, you will be treated according to your doctor's recommendations for appropriate clinical care. We may need to share the results of research testing with your doctor. We will discuss with your doctors whether you need to change dosage or stop the study medication.

Cancers

Drugs that affect the immune system may increase the risk for cancer. Individual events of cancer have been reported in people taking baricitinib. The types of cancer that were most frequently reported were skin cancer, including melanoma and non-melanoma cancer types, lung cancer, and breast cancer. Risk of overall cancer is increased when taking baricitinib.

Blood Clots in the Blood Vessels

Some people who received baricitinib developed blood clots in the blood vessels of their legs, which may then dislodge and travel to the lungs. This complication may be fatal. Baricitinib should be used with caution in people who are at high risk for blood clots in their blood vessels. Specifically, older patients (50 years of age or older) with risk factors for heart disease who were treated with medications similar to baricitinib had an increased risk of blood clots in the blood vessels.

Tell your doctor if you have had blood clots in the veins of your legs or lungs in the past. Baricitinib will be stopped if signs or symptoms of blood clots develop.

Cardiovascular events

Older patients (50 years of age or older) with risk factors for heart disease who were treated with medications similar to baricitinib had an increased risk of major medical events involving the blood vessels of the heart and brain, including heart attacks and stroke. In some cases, these medical events caused sudden death from heart attack or stroke. These events have not been fully studied in older patients taking baricitinib. Taking baricitinib has not been shown to increase your chance of having heart related problems such as heart disease, heart attack, heart failure, or stroke, at this time.

Digestive System

Small increases in blood tests related to the liver were common in people taking baricitinib during trials. These increases were also seen when baricitinib was given along with another medicine (methotrexate) used to treat arthritis. This medicine (methotrexate) is known to be associated with effects on the liver.

Stomachache and upset stomach have been commonly reported with baricitinib. Upset stomach has usually been seen when first starting baricitinib. In most people, the upset stomach got better with continued baricitinib use.

Some people using baricitinib get tears in their stomach or intestine. This happens most often in people who also take medicines such as nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids.

Please seek medical care immediately if you experience new onset of abdominal pain, fever, chills, nausea, or vomiting.

Blood Tests

Higher amounts of cholesterol in the blood (good and bad cholesterol) were very common in people who took baricitinib. Higher amounts of fat in the blood were uncommon. These changes have not been associated with an increased risk of stroke, heart attack, or blood clots.

A higher number of parts of the blood that aid in clotting (blood platelets) were commonly reported in people taking baricitinib. These increases have not been associated with an increased risk of stroke, heart attack, or blood clots.

Small changes in blood tests related to muscle have been seen uncommonly in people treated with baricitinib. In most people with these changes, the changes were temporary. Although there was no clear link with any muscle problems, symptoms such as muscle aches and pain were reported by some people. In people with atopic dermatitis, small changes in blood tests related to muscle were seen commonly.

Decreases in the number of white blood cells were uncommonly reported with baricitinib, which could affect the body's ability to fight infection.

Lower counts of red blood cells (anemia) have been described in people taking baricitinib.

Increases in creatinine, a measure of how well the kidneys work, have been described in people taking baricitinib. Increased creatinine may be a marker of worse kidney function.

Pregnancy and Breastfeeding

Animal studies of baricitinib have shown harmful effects to both the mother and unborn babies, including a harmful effect on the bones of the babies. There is little information about the use of baricitinib in pregnant women. The available information has not shown any harmful effects on the unborn baby, but the number of pregnancies in people is too small to know the risks to the unborn baby.

If you are a woman or a man who can have children, you must not become pregnant or father a child while taking baricitinib. You should use appropriate precautions to avoid pregnancy during the study and for at least 1 week after you take your last dose of baricitinib or as defined in the study-specific protocol.

Your doctor may provide other guidelines for how long to wait after taking your last dose of baricitinib before trying to get pregnant. Women who are pregnant should not take baricitinib.

In one animal study, baricitinib was present in breast milk. Women who are breastfeeding should not take baricitinib.

Weight Gain

People taking baricitinib gained on average 1 kg of weight over 16 weeks. Some people had weight gain greater than 1 kg.

Skin

Skin rash was commonly reported, while hives and swelling of the face or lips were uncommonly reported. Some of these reactions occurring in the first days after starting baricitinib could be due to an allergic reaction to baricitinib.

Allergic reactions may include rash; swelling of your lips, tongue, or throat; hives (raised red patches of skin that are often very itchy); itching; swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; or unusual hoarseness.

An allergic reaction is a condition in which the immune system reacts abnormally to a substance. Some allergic reactions may be life-threatening. Please call 9-1-1 in the event of an emergency.

Acne can uncommonly occur in people taking baricitinib. In people with atopic dermatitis, acne was seen commonly.

Headache

Headache was commonly reported during the first months of treatment.

Vaccinations

You should not receive live vaccines while taking baricitinib. Live vaccines typically include: Measles, mumps, rubella (MMR combined vaccine), Rotavirus, Smallpox, Chickenpox, and Yellow fever.

Additional Information

Your doctor will frequently check your general health. Your doctor will also check your white blood cell count, platelet count, kidney function, liver function, blood tests related to muscles, and levels of blood cholesterol and fat throughout your participation in the study.

You should report any changes in your medical condition to your doctor. Make sure you tell your doctor about any medicine that you take, including prescription medicine, over-the-counter medicine, and herbal products.

Baricitinib is removed from the body by the kidneys. People with reduced kidney function do not remove baricitinib as quickly as those with normal kidney function. People with reduced kidney function may require a lower dose of baricitinib.

Eli Lilly and Company (the drug manufacturer) regularly reviews all important safety information for their study drugs. As of 13 August 2022, a total of 14,233 people have taken one or more doses of baricitinib in clinical studies. This number includes healthy people and people with arthritis, lupus, dermatitis, diabetic kidney disease, psoriasis (condition in which skin cells build up and form patches of dead skin and itchy red patches), alopecia areata (sudden hair loss that starts with one or more circular bald patches), primary biliary cholangitis (autoimmune disease that causes progressive destruction of the bile ducts), COVID-19, and children and young adults with very rare diseases. Baricitinib is being sold in many countries around the world. Baricitinib is also indicated for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal (artificial) life

support. It is estimated that 1,322,100 people have taken baricitinib worldwide as of 31 July 2022.

The event rates are described as follows:

Very Common **(1 or more out of 10 patients)**	**Common** **(1 or more out of 100 patients)**	**Uncommon** **(1 or more out of 1000 patients)**
· higher amounts of cholesterol (good and bad cholesterol) in the blood · upper respiratory tract infections (including symptoms similar to the common cold: cough, stuffy or runny nose, scratchy or sore throat, sneezing)	· increases in blood markers related to the liver[a] · higher number of blood platelets (parts of the blood that aid in clotting) · increases in blood markers related to the muscle · cold sores · shingles (adult "chicken pox") · urinary infection · upset stomach · stomachache · rash · headache[b] · acne	· lower number of white blood cells, including special types of white blood cells (blood cells that fight infections)[a,b,c] · higher amounts of fat in the blood · blood clots in the lungs[a,b] · blood clots in the veins[a] · hives · swelling of the face · weight gain

a In patients treated with baricitinib in COVID-19 trials, increases in blood markers related to the liver were very common, while blood clots in the lungs, blood clots in the veins, and lower number of white blood cells were common.

b In children and adolescents treated with baricitinib in a juvenile idiopathic artritis clinical trial, headache was very common, and lower number of white blood cells was common. Blood clots in the lungs was common and noted in 1 adolescent

c In children and adolescents treated with baricitinib in a pediatric atopic dermatitis clinical trial, lower number of white blood cells was common.

Additional Risks Specific to Children and the Elderly

Children

In a study of animals with an age similar to young children, lower body weights were seen in animals. These animals were on higher doses of baricitinib than would be taken by people in a study.

These animals also had changes in their bones such as increased bone thickness and changes in bone development at doses of baricitinib similar to what would be taken by people in a study.

Your growth will be carefully monitored during the study through measurements of height and weight, blood tests and x-rays of the hand.

A very small number of children have taken baricitinib. Based on the number of children that have received baricitinib, it is not possible to know if there is a difference in unwanted effects seen in children compared to adults.

Elderly

Only a small number of people who are 75 years old or older have taken baricitinib. Based on the data in people 65 years old or older, unwanted effects appear to be the same as those seen in younger adults.

Other Potential Risks

There is no promise that your health will get better in this research study. It might stay the same or it might get worse. At any time during this research study, you may experience a return or worsening of your symptoms.

In addition to the side effects already described, baricitinib and the research study procedures may have other unknown risks.

There may be unknown risks of possible harmful interaction with other medication you may be taking.

The research study drug should never be given to other people.

Risks associated with the physical examination and vital signs:

There are no physical risks but you might experience momentary embarrassment or discomfort. The exam is similar to those that are performed as part of routine medical care.

When blood pressure is taken during physical exams, the blood pressure cuff may cause discomfort or bruising to the upper arm.

When eyes are examined, you may experience discomfort from the brightness of the light used to examine the eyes.

Risks associated with neurologic function testing:

There are no physical risks but you might experience momentary embarrassment or discomfort. The exam is similar to those that are performed as part of routine medical care.

Risks associated with drug interactions:

Some medications may cause unwanted effects when combined with baricitinib or may make it difficult to tell whether or not baricitinib is working. Please tell the study doctor about all of the medicines you are taking. This includes prescription and over-the-counter drugs, supplements, homeopathic, alternative, or herbal medicines, and vitamins. You should also contact the study doctor before starting a new medicine or stopping or changing any of your current medicines. It is important to maintain stable doses of the

medications you take. We will go over which medicines you are allowed and which you are not allowed to take during the study.

In particular, probenecid, used to treat gout, may increase the levels of baricitinib in your blood. Medicines which are used to control the body's immune response, such as azathioprine, tacrolimus or cyclosporine, or rituximab, should not be used with baricitinib.

Risks associated with urine tests:

There are no physical risks but you might experience momentary embarrassment or discomfort. The test is similar to those performed as part of routine medical care.

Risks associated with blood tests, HIV testing, and IFN signaling:

Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection. Additionally, being tested for hepatitis, tuberculosis and HIV may cause anxiety. A positive test means that you may have been infected with the virus. Receiving positive results may make you very upset. If other people learn about your positive test results, this may affect your ability to get insurance or employment. If your test is positive we will refer you to someone who can explain what this means for your future medical care. If your test is negative, there is still the possibility that you could be infected and test positive at some time in the future. Also, it is always possible that the test results could be wrong. Pennsylvania state law requires that all positive hepatitis, tuberculosis and HIV test results be reported to the state.

Risks associated with an IV catheter:

Placing an IV may cause some pain, and bleeding or bruising at the spot where the needle enters your body. Rarely, it may cause fainting. The longer an IV catheter is left in place, the more common it is for redness or infection to develop.

Risks associated with ionizing radiation/x-ray:

This study involves exposure to radiation from a chest x-ray and hand/wrist/fingers x-rays. You will therefore receive a radiation dose. This dose is not necessary for your medical care. You will get the radiation only because you are taking part in this study. Radiation can increase the risk of cancer after many years but at a dose much higher than you will get. Because of the low dose of radiation, it is very likely that you will see no ill effects.

Risks associated with an echocardiogram:

Echos are very safe. The gel may feel cold when it is first placed. Some people with sensitive skin can develop a rash from the gel.

Risks associated with Electrocardiograms (ECG) :

ECGs measure the electrical activity of the heart. Sticky pads and wires will be attached to the chest. These sticky pads may cause a temporary skin reaction or skin irritation. In addition, these pads may cause some discomfort when they are removed, similar to the pulling sensation associated with the removal of a Band-Aid.

Risks associated with decreasing or stopping study drug during the course of the study:

In some patients who stopped or decreased baricitinib, AGS related disease symptoms got worse after drug discontinuation. It is important to speak to study staff before decreasing or stopping the study medication.

Breach of Privacy and Confidentiality:

As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality.

At the time of participation, each participant will be assigned an identification number. This number will be used on data collection forms, blood samples, and in the database instead of names and other private information. A separate list will be maintained that will link each participant's name to the research identification number for future reference and communication.

Are there any benefits to taking part in this research study?

You might benefit by taking baricitinib. It is possible that baricitinib will help to improve your symptoms of AGS. However, we cannot guarantee or promise that you will receive any direct benefit by participating in this research study.

You may receive information from physical examinations, laboratory tests, or other testing that is done in this research study but these tests may not have any impact on your health.

The knowledge gained from this research study may help other people with AGS.

Do you need to give your consent in order to participate?

If you decide to participate in this research study, you must sign this form. A copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research study subject when making your decision about participating in this research study. You will need to follow the research study doctor’s instructions, keep all research study appointments, and take baricitinib as directed.

What happens if you decide not to take part in this research study?

Participation in this research study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled. Tell the doctor if you are thinking about stopping or decide to stop.

Can you stop your participation in the research study early?

You can stop being in the research study at any time. You do not have to give a reason. If you stop being part of this research study, the study doctor or one of the staff members will talk to you about any medical issues regarding the stopping of your participation.

Can the research study doctor take you out of the study early?

The doctor or CHOP can remove you from the research study without your consent for any reason. These reasons may include:

- if participating becomes harmful to your health
- if you do not follow the research study doctor's or staff members' instructions
- if the research study is stopped

What choices do you have other than this research study?

There are options for you other than this research study including:

- Getting treatment with other medications or care for your inflammatory condition without being in a research study
- Getting treatment with commercially available baricitinib. Baricitinib is available by prescription in the United States, even though not approved for inflammatory disease in children at this time.
- Getting no treatment

The doctor will discuss with you the risks and benefits of the alternative treatments.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research study, health information about you will be collected. This will include information from medical records, procedures, interviews and tests. Laboratory test results will appear in your medical record with the exception of research-only tests. The results of IFN gene signaling tests will not be entered into your medical record. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Personal information may be disclosed if required by law.

The results of this research study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research study, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP;
- People from agencies and organizations in the US and other counties that perform independent accreditation and/or oversight of the research study; such as the Department of Health and Human Services, Office for Human Research Protections;
- Representatives of Eli Lilly and Company and their contracted business partners who have donated baricitinib for this research study;
- The Food and Drug Administration;

- Your primary physician will be contacted if, during the course of the treatment protocol, the research study doctor learns of a medical condition that needs immediate attention;
- Public health authorities that are required by law to receive information for the prevention or control of disease, injury or disability;
- A Data Safety Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research study. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this research study. Your permission to use and share the information and data from this study will continue until it ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you tell the investigator in writing.

Dr. Adeline Vanderver
The Children's Hospital of Philadelphia
Division of Neurology
Abramson Research Building
Philadelphia, PA 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research study. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the research study.

Additional Information

You will be informed if changes to the research study are needed to protect your health. You will be told about any new information that could affect your willingness to stay in the research study, such as new risks, benefits or alternative treatments.

Financial Information

CHOP can only pay for the procedures related to taking baricitinib. These include the study visits with the research team, safety blood draws and procedures done at CHOP, PK studies, interferon studies and pregnancy testing.

Baricitinib will be provided to you free of charge.

While you are in this research study, the cost of your usual medical care for AGS – procedures, medications and doctor visits – will continue to be billed to you or your insurance. If some of these clinical visits occur at CHOP, these will be billed to your insurance.

Will there be any additional costs?

You will be responsible for some expenses related to this research study, such as transportation, parking, meals, or other expenses related to visits.

Taking baricitinib may require you to take additional medications, such as antibiotics or other medications to manage side effects. You or your insurance company would be required to cover these costs.

Clinical care procedures to monitor cardiac function will not be covered by the study. You or your insurance company would be required to cover these costs.

CHOP has studies to help uninsured and underinsured families see if financial assistance is available. If you need financial assistance, please let a member of the study team know.

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

You will not receive any payments for taking part in this research study.

We may share your specimens and data with third parties (other researchers/institutions or for profit companies). You will not receive any financial benefit from the use of your specimens or data.

Who is funding this research study?

CHOP, Eli Lilly and Company and Pennsylvania Department of Health are funding this research study. Eli Lilly and Company is a drug company that makes the medication being studied in this research project. Eli Lilly and Company is giving the medication to CHOP. The physicians overseeing your care during this research study are not being paid for their participation.

The results of the study will be reported to Eli Lilly and Company. If the study shows that the study drug may be useful for a new purpose, this could benefit Eli Lilly and Company financially.

What if you have questions about the research study?

If you have questions about the research study, call the study doctor, Dr. Vanderver at (215) 590-1719. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies and makes sure subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

A description of this research study 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.

What happens if you are injured during the research study?

If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research.

You and your insurance company will be billed for the costs of any care or injuries.

If you think you have been injured from taking part in this research study, call Dr. Vanderver at (215) 590-1719. She can go over things with you, let you know of resources that may be available and give you information on what you need to do.

In case of injury resulting from this research study, you will not lose any legal rights by signing this form.

What will be done with my data and specimens when this study is over?

We will use and may share data and/or specimens for future research. They may be shared with researchers/institutions outside of CHOP. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data and/or specimens, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

The information and samples will be given a unique code and may include information that can identify you. We will keep a list at CHOP that links the specimen back to you. Information that can identify you or the samples may be kept permanently in a computer database at CHOP.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research Study *(English speaking subjects only)*

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and if you are giving permission for a child or consent for an adult to participate in this research study, you are legally authorized to consent to the child's or adult's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this research study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject	Date
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian ☐ Legally Authorized Representative
Signature of Authorized Representative	Date

Assent to Take Part in this Research Study

For children (or adults with diminished capacity) capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Conducting Assent

_____ _____
Signature of Person Conducting Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children (or adults with diminished capacity) unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Conducting Assent

_____ _____
Signature of Person Responsible Date

STUDY SUMMARY SIGNATURE PAGE
(For Non-English speaking subjects only)

Consent to Take Part in this Research Study and Authorization to Disclose Health Information

Name of Subject

Name of Authorized Representative (if different than subject)

Relation to subject:
☐ Parent ☐ Legal Guardian
☐ Legally Authorized Representative

The research study and consent form have been explained to the subject or parent/legal guardian/legally authorized representative.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's/legally authorized representative's questions, they have agreed to take part in this research study and they are legally authorized to consent to their, their child's, or the adult's participation. They have also agreed to let CHOP use and share the health information as explained above. If they don't agree to the collection, use and sharing of the health information, they cannot participate in this study.

Person Obtaining Consent

Signature of Person Obtaining Consent

Date:

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Witness/Interpreter

Signature of Witness/Interpreter

Date:

Assent to Take Part in this Research Study *(Non-English Speaking Subjects)*

For adults with diminished capacity capable of **providing assent:**

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

For adults with diminished capacity unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Conducting Assent

_____ _____
Signature of Person Responsible Date

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining assent was presented to the subject if they were capable of providing assent in a language preferred by and understandable to the subject; and
- The subject's questions, if they were capable of providing assent, were interpreted and the responses of the person obtaining assent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining assent (including responses to the subject's questions) and responded affirmatively, if they were capable of providing assent.

_____ _____
Name of Witness/Interpreter Signature of Witness/Interpreter

Date: _____

CONSENT APPENDIX 1: Information about Samples Collected During this Study

What samples will be collected?	Why will samples be collected?	How long will samples be stored?	Are these samples linked to my identity?
Limited Use Samples: Blood Urine	• To see if you meet requirements to be in this Study • To check your overall health (standard of care tests, Adverse Event collection) • To see if you are responding to the Study drug (disease response to Study drug) • To monitor the levels of the Study drug in your blood (PK samples)	• Routine blood and urine specimens may be stored indefinitely for future research to better understand AGS	• Yes but with a unique identifier to protect your confidentiality

All samples collected for laboratory tests will be destroyed within the planned time unless laws, regulations, or international laboratory certification standards require a longer retention period. The results of these tests will be kept confidential and shared only as required by law.

CONSENT APPENDIX 2: Study timeline*

	Screening	Baseline	Itinial Dosing	Treatment						Early Termination	Safety Closeout
Visit number	Required	1	2		4		201	204, 207, 210	212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231	ET	
	Optional			3		5		202, 203, 205, 206, 208, 209, 211	212A, 213A, 214A, 215A, 216A, 217A, 218A, 219A, 220A, 221A, 222A, 223A, 224A, 225A, 226A, 227A, 228A, 229A, 230A		801
Weeks from enrollment		4 to .5	0	2	4	8	12	16 to 52	60 to 288	—	292
Number of days at visit		28 to 2	Variable	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5

* If you decide to continue the study because commercial supply is not available, your study schedule will continue as the one described above, with visits every three months, alternating on-site and phone assessments.