UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:	A phase II, single-arm, open-label, multi-center study of Sirolimus in previously treated idiopathic multicentric Castleman disease
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Research Study Summary for Potential Subjects

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The research study is being conducted to determine the effects of the study drug (sirolimus) in adults who have been diagnosed with idiopathic multicentric Castleman Disease (iMCD) and are either unable to tolerate siltuximab or tocilizumab, or have failed, relapsed, or are refractory to this treatment.

If you agree to join the study, you will be asked to take sirolimus daily for 12 months.

Your participation will last for up to approximately 73 weeks, or about 15 months (12 months active study participation, plus 1 follow-up phone call 3 months later), with approximately 17 study visits; 6 of the study visits must occur at the study site. The other visits may occur at a local medical facility or blood draw facility close to you. The information collected from you may be held indefinitely in a research database.

You may or may not benefit from being in this study and taking sirolimus. It is possible that you may get better, stay the same, or get worse. Information from this study may be used to better understand iMCD and how to diagnose and treat it in the future. The most common risks of taking sirolimus are peripheral edema (swelling in your arms or legs), high cholesterol and triglycerides, decreased kidney function, constipation, high blood pressure, abdominal pain / diarrhea, headache, acne, and pain or swelling in the joints.

Please note that there are other factors to consider before agreeing to participate, such as additional procedures, alternative treatments (other drugs and chemotherapies), use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being invited to participate in a clinical research study because you have been diagnosed with idiopathic multicentric Castleman Disease (iMCD) and you are either unable to tolerate siltuximab or tocilizumab, or you have failed, relapsed, or are refractory to this treatment (the medication did not work or is no longer working). Your participation is voluntary, which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the investigator and/or the research team about this form. If you decide to participate, you will be asked to sign this form. Your doctor may be an investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

What is the purpose of this research study?

The main purpose of this clinical trial is to determine the effects of the study drug (sirolimus) in adults diagnosed with iMCD. The study will evaluate how well the drug is tolerated and its effects on participants' iMCD symptoms.

Sirolimus is approved by the Food and Drug Administration (FDA) for the prevention of organ transplant rejection and to treat a rare lung disease. The use of the sirolimus in this study is experimental, which means that the drug is being investigated for a new use in iMCD.

Reviews of your medical record information, blood tests, imaging studies (CTs or PET scans), physical exams and information you tell the study doctor will be used to determine how your iMCD is responding to the study drug.

How long will I be in this study? How many other people will be in the study?

If you are eligible, your participation will last for up to approximately 73 weeks, or about 15 months (12 months active study participation, plus 1 follow-up phone call 3 months later), with approximately 17 study visits; 6 of the study visits must occur at the study site. The other visits may occur at a local medical facility or blood draw facility close to you.

This clinical trial will be performed in three centers with a total of up to 40 subjects. Men and women aged 18-80, as well as children 2 years of age or older, with iMCD who meet eligibility criteria will be included in this study.

The three centers participating in this study are the University of Pennsylvania, the University of Arkansas for Medical Sciences, and the Children's Hospital of Philadelphia.

What am I being asked to do?

Before you can start the study, the study doctor or study staff will talk to you about the study. If you agree to participate in this study, you have to sign this informed consent form before the study doctor or study staff can do any study-related procedures. If you decide to participate in this study and are found eligible, you will start taking the study drug within the next 0-5 days.

To determine if you are eligible for the study, the study team will use information from your medical history and from tests, procedures, and physical examinations that took place at your past clinical appointments and during the screening phase. If you qualify for the study, you will be asked to complete the activities and procedures described in the following paragraphs.

After completing the in-person screening visit, you will be asked to come back to the clinic for 6 in-person visits and to complete 9 remote visits, which include research blood draws and telephone contacts. The 6 in-person visits will occur within a week of the screening phase, and then 1 month, 3 months, 6 months, 9 months, and 12 months after you start taking the study drug. You will need to travel to your study center for each of these visits. Each in-person visit will take up to one hour of your time in addition to your regular clinical care and each telephone contact will take approximately 30 minutes or less. At the first visit, you may have up to 7 tablespoons of blood drawn for research purposes. At each follow-up visit, you may have up to 3.5 tablespoons of blood drawn for research purposes.

The study drug you will receive is in the form of tablets, to be taken by mouth. You will be asked to take a loading dose on the first day of taking the drug. A loading dose is an initial higher dose of a drug that is given at the beginning of a course of treatment before dropping to a lower maintenance dose. A loading dose is used for drugs that leave the body relatively slowly. This loading dose will occur during the baseline visit or within a few days of the baseline visit. Starting 1 day after you take the loading dose, you will be asked to take a lower dose once a day, which may be increased or decreased by your physician, until you have reached the appropriate level in your blood and then you will be continued at that dose. You should take the study drug in the morning at the same time each day. The study drug can be taken with or without food. If you prefer to take the study drug with food, then you should always take it with food. If you prefer to

take the study drug without food, then you should always take it without food. You should not drink grapefruit juice while you are on sirolimus. Your sirolimus dose should not be taken on the mornings that you are having in-person or remote visits. You should take your sirolimus dose immediately after your visits. You will be instructed to record all sirolimus doses taken daily in a study medication diary, provided by the study team at Baseline, and to bring it with you to every in-person study visit (1, 3, 6, 9, and 12 Month Visits). Research blood draws will be taken approximately 5 days and then 2 weeks after you take the initial dose, and then monthly until the end of your study participation. Nine of the research blood draws may be completed remotely.

The study team will use information from tests and procedures that you are having done as standard-of-care. This means that you would have had these procedures done whether or not you were part of this research study, as part of your regular medical care. Laboratory test results, radiology procedures (computerized tomography (CT) or positron emission tomography (PET/CT), and physical exam findings are examples of standard-of-care procedures that will be used by the study team by getting the information from your medical record.

If you experience ascites and undergo a clinical procedure to remove excess fluid, we would collect and store some of the fluid for further research analysis. We would not be collecting any additional fluid beyond what is being measured for clinical purposes.

The schedule and procedures of required visits and telephone contacts for this study are explained below. A table outlining the study visits and telephone contacts appears on page 7 and 8 of this form.

Visit 0 - Screening Phase

Before any study-related procedures are performed, you will be asked to read and sign this consent document. During the screening phase, the study doctor or study staff will discuss the study with you, review your medical history and personal information, and ask you about medications you are taking. If you are female and able to have children, you will need to take a urine pregnancy test. The study team will conduct the following standard-of-care procedures if they occurred more than 4 weeks prior to the screening visit: standard diagnostic laboratory tests, vital signs, radiological imaging (PET/CT or CT), and lipid panel.

If you are eligible to participate in this study based on the screening results, the study team will contact you to schedule a Baseline visit within 7 days of the screening visit.

Visit 1 - Baseline

The study doctor or study staff will review your medical history and ask you about medications you are taking. The study team will conduct the following standard-of-care procedures if they occurred more than 4 weeks prior to Visit 1: physical exam, including performance score, and vital signs.

If you meet the study requirements, the study staff will dispense the sirolimus loading dose. They will also provide you with several weeks' worth of sirolimus. You will be asked to take the next dose on the day after you take the loading dose. The next dose will be a lower dose and may be adjusted by your doctor to achieve the optimal dosing for you.

You will also have blood drawn for research purposes. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time.

You will be asked to provide an optional fecal sample.

Your next two study site visits will be scheduled approximately 5 days and 2 weeks after your baseline visit. You will be provided with blood draw tubes for you to use at these visits if you plan to have your blood drawn at a facility that is local to you.

At every in-person visit after this you will be asked to bring all remaining study drug, and all bottles/ packaging (even if they are empty), back to your doctor.

Visits 2, 3, 5, 7, 8, 10, 11, 13, and 14 - Remote Visits / Telephone Contact

These visits occur 5 days, 2 weeks, and then 2, 4, 5, 7, 8, 10, and 11 months after you start taking the study drug. During these visits, you will be contacted by phone by the study staff. The study staff will evaluate your general health and ask about the medications you take. They will ask you questions about how you have been feeling to investigate whether you have had any side effects and to evaluate your response to the study drug. They will also ask you questions about how consistently you have been taking the study drug. At Visit 3 (Week 2), you may be asked to provide an optional fecal sample.

You will also be asked to visit your local medical provider or facility where a research blood draw will be conducted. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time. You will be reminded to provide the technician drawing your blood with the research blood tubes you were given at your last visit. You will be asked to ship the research blood tubes using the pre-labeled shipping materials provided by the study staff after the blood draw.

Visits 4, 6, 9, and 12

These study visits occur 1, 3, 6, and 9 months after you start taking the study drug. It is highly encouraged that you return to the study site, but the study doctor may allow one or more of these visits to occur remotely. At these visits, the study staff will have you take a urine pregnancy test (if applicable), review your medical history data and laboratory tests, and evaluate your general health. They will also ask about the medications you are taking. The study staff will ask you questions about how you have been feeling to investigate whether you have had any side effects and to evaluate your response to the study drug. You will also have blood drawn for research purposes. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time. At visit 9 (6 months after you start taking study drug), you will be asked to provide an optional fecal sample.

You must bring all of your study drug and bottles/packaging (even if they are empty). You will receive additional study drug, enough for three more months of treatment, from the study staff.

If the study visit occurs remotely, you will need to speak to the study doctor and study staff by phone or videocall, get a CT or PET scan at a local provider, and have blood drawn remotely.

You will also be asked to visit your local medical provider or facility where a research blood draw will be conducted. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time. You will be reminded to provide the technician drawing your blood with the research blood tubes you were given at your last visit. You will be asked to ship the research blood tubes using the pre-labeled shipping materials provided by the study staff after the blood draw. You will also need to provide the name and location where your CT or PET scan occurred, and provide permission for the study team to receive your CT or PET images and radiology report.

You will also be provided with blood draw tubes and shipping supplies for you to use at your next remote visit (if applicable).

Visit 15 - End of Treatment Visit

This visit occurs 12 months (1 year) after you start taking the study drug. It is highly encouraged that you return to the study site, but the study doctor may allow this visit to occur remotely. At this visit, the study staff will have you take a urine pregnancy test (if applicable), review your medical history data and laboratory tests, and evaluate your general health. They will also ask about the medications you are taking. The study staff will ask you questions about how you have been feeling to investigate whether you have had any side effects and to evaluate your response to the study drug. You will also have blood drawn for research purposes. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time.

You must also bring all of your study drug and bottles/ packaging (even if they are empty).

If the study visit occurs remotely, you will need to speak to the study doctor and study staff by phone or videocall, get a CT or PET scan at a local provider, and have blood drawn remotely. You will also be asked to visit your local medical provider or facility where a research blood draw will be conducted. If you are already having blood drawn for your clinical care, the research blood may be collected at the same time. You will be reminded to provide the technician drawing your blood with the research blood tubes you were given at your last visit. You will be asked to ship the research blood tubes using the pre-labeled shipping materials provided by the study staff after the blood draw. You will also need to provide the name and location where your CT or PET scan occurred, and provide permission for the study team to receive your CT or PET images and radiology report. You may need to ship study drug back to the study site.

If you chose to discontinue or were withdrawn from the study before reaching visit 14 you will still be asked to complete an End of Treatment Visit.

Visit 16 - Follow- Up Telephone Contact

This phone call will occur 12 weeks after Visit 15. During this phone call, the study staff will evaluate your general health and ask again about the medications you take. They will ask you questions about how you have been feeling to investigate whether you have had any side effects and to evaluate your response to the study drug.

This will be your last scheduled study contact.

Other Study Visits

If you have moderate or serious side effects that are concerning to your study doctor, or if the study doctor feels it would be best, you may be asked to re- test a laboratory value or come to the clinic for further safety evaluation.

The study staff may contact you in between study visits to schedule appointments, send reminders, or follow up on your health.

Contact Regarding Other Research Studies

You may be contacted regarding other research opportunities. You may choose to decline any research study, and this decision will not affect your clinical care or your participation in this study.

Study Phase	**Screening**	**Baseline**	**Intervention Phase**							
Study Visit Number	**Screening[1]**	**1[1]**	**2[2]**	**3[2]**	**4[1]**	**5[2]**	**6[1]**	**7[2]**	**8[2]**	**9[1]**
Study Days	-28 to 0 Days	-7 to 0 Days	5 Days	14 Days	1 Month	2 Months	3 Months	4 Months	5 Months	6 Months
Diagnostic Laboratory Tests*	x									
Physical Exam*		x			x		x			x
Vital Signs*	x	x			x		x			x
Radiological Imaging*	x						x			x
Lipid Panel	x	x			x		x			x
Review of concomitant medications*	x	x								
Confirmation subject meets enrollment criteria	x	x								
Informed Consent	x									
Pregnancy Test (urine)	x				x		x			x
GUID assigned		x								
Research blood draw		x	x	x	x	x	x	x	x	x
Fecal sample collection (optional)		x		x						x
Recording of Demographic information	x									
Recording of medical history data, medications, possible AEs and Laboratory Tests, as available		x	x	x	x	x	x	x	x	x
Completion of Patient Evaluation Form and eligibility confirmation by Lead PI	x	x								
Dispensing of sirolimus loading dose		x								
Dispensing of sirolimus daily dose		x			x		x			x
Assess possible AEs, study drug compliance, and medication changes			x	x	x	x	x	x	x	x
Sirolimus Trough			x	x	x		x			x
Standard of Care Laboratory Test*					x		x			x
Return of any non-consumed sirolimus					x		x			x
Sirolimus pill count					x		x			x
Intermediate assessment of primary objective							x			x
Final assessment of primary objective										
Follow Up telephone questionnaire										

* Standard of Care for iMCD.
1. Visit must be done in-person at the study site.
2. Visit may be done remotely by phone and at a local blood draw facility (if applicable).

Study Phase	**Intervention Phase**						**Early Termination Visit**	**Follow-up Phase**
Study Visit Number	**10[2]**	**11[2]**	**12[1]**	**13[2]**	**14[2]**	**15[1]**		**16[2]**
Study Days	7 Months	8 Months	9 Months	10 Months	11 Months	12 Months		15 Months
Diagnostic Laboratory Tests*								
Physical Exam*			x			x	x	
Vital Signs*			x			x	x	
Radiological Imaging*			x			x		
Lipid Panel			x			x		
Review of concomitant medications*								
Confirmation subject meets enrollment criteria								
Informed Consent								
Pregnancy Test (urine)			x			x	x	
GUID assigned								
Research blood draw	x	x	x	x	x	x	x	
Fecal sample collection (optional)								
Recording of Demographic information								
Recording of medical history data, medications, possible AEs and Laboratory Tests, as available	x	x	x	x	x	x	x	
Completion of Patient Evaluation Form and eligbility confirmation by Lead PI								
Dispensing of sirolimus loading dose								
Dispensing of sirolimus daily dose			x					
Assess possible AEs, study drug compliance, and medication changes	x	x	x	x	x	x	x	x
Sirolimus Trough			x			x	x	
Standard of Care Laboratory Test*			x			x	x	
Return of any non-consumed sirolimus			x			x	x	
Sirolimus pill count			x			x	x	
Intermediate assessment of primary objective				x				
Final assessment of primary objective						x		
Follow Up telephone questionnaire								x

* Standard of Care for iMCD.
1. Visit must be done in-person at the study site.
2. Visit may be done remotely by phone and at a local blood draw facility (if applicable).

What are the possible risks or discomforts?

Some possible risks that may be associated with participation in this study are specifically disclosed below; however, there may be additional harmful consequences that are not discussed below or not yet known.

As in any clinical research study, there is the chance of experiencing side effects to the study drug or risks and discomforts from the study procedures. However, your doctor will follow you closely and keep track of any unwanted effects or any problems.

Sirolimus risks

Sirolimus is approved by the FDA for conditions other than iMCD, so the risks are well-studied. The most common risks of sirolimus (occurring in ≥ 20% of patients) are peripheral edema (swelling in your arms or legs), high cholesterol and triglycerides, decreased kidney function, constipation, high blood pressure, abdominal pain / diarrhea, headache, acne, and pain or swelling in the joints.

Less common risks include rash, weight gain, muscle/joint pain, tremor, angioedema (rapid swelling), low white blood cell count, high or low platelet count, fluid accumulation, impaired wound healing, and protein in urine.

You should inform the study doctor if you experience any of these side effects.

Rare but serious side effects include allergic reaction (may be life threatening), decreased red and white blood cells generated in bone marrow, decreased liver function, lymphoma or malignancy (cancer), destruction of red blood cells, interstitial lung disease (scarring of the lungs), and hemolytic uremic syndrome/thrombotic thrombocytopenic purpura (conditions of low blood cell counts, low platelet counts and kidney damage). You may be at an increased risk for opportunistic infections, including polyoma virus infections. Polyoma virus infections in patients taking medications like sirolimus may have serious, and sometimes fatal, outcomes. If you experience any of these rare but serious side effects mentioned above, please inform your doctor or the study staff immediately or go to the nearest emergency room.

Blood draw risks

During the study, your blood will be drawn to perform a variety of laboratory tests and for research purposes. The risks of drawing blood include pain, bruising and in rare instances, infection. Some subjects may experience nausea and dizziness after the blood draw. Standard care will be taken to avoid these complications. Efforts will be made to draw blood at the same time that you are having blood drawn for your clinical care.

Risk of loss of confidentiality

To help ensure confidentiality, your samples will be coded and stored in a secured facility. However, it is possible that results from this study will be accessed by people who are not authorized to do so.

Reproductive risks

Because of the effects of the study drug, there could be serious harm to unborn children or children who are breast-feeding while you are on the study drug. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. There is no evidence for long term reproductive risks for more than 12 weeks after sirolimus is discontinued.

Both male and female subjects are required to use contraception during the study and for at least 12 weeks after stopping the study drug.

If you are a woman who can become pregnant, you should not become pregnant while you are taking the study drug. You will be given a urine pregnancy test before entry into the study to make sure you are not pregnant. Afterward you will be tested every 1 – 3 months while you are in the study. You are asked to use a medically accepted method of birth control (such as condoms, diaphragm, intrauterine devices (IUDs) or hormone therapy) while you participate in the study. If you are a man, your sexual partner(s) should not become pregnant while you are taking it. Contraceptive protection should be continued for at least 12 weeks after the study drug is stopped. Your study doctor will review your birth control method with you and advise you on what is acceptable in order to participate in the study.

If you are a woman who becomes pregnant or if you are a man whose sexual partner becomes pregnant, you must tell the study doctor immediately. Your doctor will tell you about any potential risks of the study medication to the pregnancy or the baby. If you are a woman, you will be required to discontinue taking the study drug. We will follow and collect data on any pregnancy of female subjects or female partners of male subjects.

If you have been postmenopausal (no longer have your period) for at least 1 year, you can participate in the study without being tested for pregnancy or without using contraceptive protection.

If you are a woman who is currently pregnant or breast-feeding, it is important that you inform the investigator because you will not be able participate in the study.

Risks of Genetic Testing

This research includes genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

If these results were inappropriately accessed by people who are not authorized to do so, very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or longterm care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

What happens when the study is over?

When the study ends, the study doctor will discuss your treatment options, including the risks and benefits of continuing to take sirolimus. If you continue taking sirolimus, the drug will no longer be provided by the research study after the study ends, so your doctor will discuss your options for obtaining the drug.

What will happen with information and biological samples collected from me?

As a part of this study, blood, tissues, or other body fluids or samples that are collected as part of your clinical care during the study period may be stored and used for research purposes if they are no longer needed for your medical care. Samples such as blood, tissue samples, and body fluids may have been collected from you before you started participating in this study. The study team may try to locate these samples if they were stored. If the samples are no longer needed for your medical care, they may be stored and used for research purposes, which may include genetic testing, possibly including whole genome sequencing. Information that is in your medical record or that you provide to the study team will also be collected.

All the samples will be processed without your name or any other information which allows your identification. Upon entry into this study, you will be given a de-identified code that will be used to label your information. Only authorized people will have access to the list of names which links your information to this code and only authorized members of the study doctor's staff will have access to your samples. Your samples will be stored at the University of Pennsylvania.

Your identifiable information and samples will be stored for future research purposes. Future researchers may receive information that could identify you. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected for this study. Identifying

information about you (name, contact information, date of birth) and medical information about you collected as a part of this study will be retained with your information and samples, but it will be coded to help protect your privacy. If your information or samples are shared with other academic institutions, researchers, or companies, they will only receive the coded information or samples.

Your information and samples may be stored and used for future research purposes for an indefinite amount of time unless you choose to withdraw your consent by the methods described later in this consent form. Possible future research may include research on Castleman Disease or similar diseases, but there are no plans to tell you about any of the specific research that will be done. We will not follow up with you to tell you about the specific research that will be done. We will not give you any results from these studies. It is possible that you may have chosen not to participate in these future research studies, had you been approached for participation.

Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality by coding your information and samples and using secure storage locations.

You will likely not directly benefit from future research with your information and samples. Research with your identifiable information and samples may help others by improving our understanding of health and disease, improving health care and making safer or more effective medical therapies, and developing new scientific knowledge.

If you have questions about the storage of your information and samples, or have changed your mind, you can contact the study team using the contact information on the first page of this form. If you change your mind, every effort will be made to destroy samples. Information that was obtained from sample analysis will not be destroyed.

By signing this consent form, you are agreeing to allow the study team to store and use samples that were collected during the study period and previously collected. You are also acknowledging that the tissue collected for this protocol may deplete (entirely use up) and in which case it will not be available for your future clinical care.

Will I receive the results of research testing?

Results from clinical laboratory tests done for research (lipid testing and sirolimus testing) will be placed in your medical record. You have the right to view your medical record. The study team will inform you if results from clinical tests require you to follow up with your primary healthcare provider.

Results from genetic testing may be returned to you if relevant to your health care, at the discretion of the study physicians.

Most non-clinical tests (tests done in the research lab) are only for research and have no clear meaning for health care. Research results will not be returned to you because they would not be relevant to your health care.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You may or may not benefit from being in this study. It is possible that you may get better, stay the same, or get worse. Information from this study may be used to better understand iMCD and how to diagnose and treat it in the future. This knowledge may be useful for future clinical studies.

What other choices do I have if I do not participate?

You can decide not to participate in this study. If you decide not to participate, it will not change the regular medical care you receive from your doctor. You should discuss alternatives with your doctor and decide whether to participate in this study. These alternatives may include other drugs or chemotherapies. If you do choose to participate, you will not be able to take these alternative drugs or chemotherapies while you are enrolled, and before you start any new medication you must bring this to the attention of your study doctor. Your study doctor will inform you should any new information about sirolimus become available during the course of the study.

Will I be paid for being in this study?

You will not be paid for participating in this study. The study drug is provided free of charge.

If you are found eligible and enroll in this study, you will be provided $50 to be used for meals and travel expenses for each visit that must occur at the study center (Screening Visit and Visits 1, 4, 6, 9, 12, and 15). Participants traveling over 100 miles to the study site may be provided with hotel and travel arrangements (flight or train tickets), if needed, for each visit that must occur at the study center (Screening Visit and Visits 1, 4, 6, 9, 12, and 15). Arrangements may be made through a third party travel service.

Payment for travel expenses will be administered using a Greenphire ClinCard, a reloadable prepaid card. There are no fees for making online or in-store purchases, cashing out the card by presenting it to a teller at any major bank, calling the automated system for balance inquires,

calling the customer service number and speaking to a live agent, or addition of funds to the card. The following activities will incur a fee to the balance on your ClinCard:

(1) not using the card or having funds added to it for more than 6 months will incur a monthly $3 fee. Every time the card is used or funds are added, this 6-month period is reset
(2) ATM withdrawals (fees vary based on location)
(3) Requesting a paper statement (instead you can always check your available balance online or by calling Customer Service)
(4) Requesting a replacement card through Customer Service will incur a $7.00 fee and take 7-10 days to receive by mail. Instead, if your card is lost, stolen or damaged, contact your study coordinator so that s/he can replace your card at no charge
(5) Requesting a check through Customer Service to remove funds from the card

Please note: In order to be compensated for your participation in this study, you must provide your Social Security Number.

Will I have to pay for anything?

There are no costs to you for taking part in this study. You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study.

You and/or your insurance provider will be responsible for routine office visits, scans and blood work that would be done whether or not you participated in this research study, if they were done as per standard-of-care. You are responsible for any deductibles or applicable co-pays that arise from these standard-of-care procedures and tests. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

You will be responsible for travel expenses if they are beyond what is described in the previous sections.

What happens if I am injured or hurt during the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you receive for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The Principal Investigator's name and phone number are listed on the first page of the consent form. As always, you should seek emergency medical treatment for any emergencies.

You are encouraged to ask questions at any time during the study. In the event you experience a side effect or have further questions about the study, please contact **Dr. David Fajgenbaum** at

(215) 614-0936 during office hours or call (215) 662-4000 to contact the hematologist/oncologist on call after hours and on weekends and holidays – inform the hematologist/oncologist on call that you are participating in a research study.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician or the study sponsor without your consent because:

- The Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision
- You have not followed study instructions
- The study Principal Investigator, the Data Safety Monitoring Board (DSMB), or the FDA has decided to stop the study

If you decide to participate, you are free to leave the study at any time. This will not affect your future treatment or your relationship with your study doctor. If you stop taking part, please tell your study doctor immediately. If you wish to or need to stop the study drug, you will be asked to come to the clinic for an Early Termination Visit. After the Early Termination Visit, no further data will be collected, except for follow-up to any serious adverse event.

Who can see or use my information? How will my personal information be protected?

The study doctor will collect information from you, from your medical record, and from your tests results. This includes information about your medical history before you started participating in this study and images from radiological procedures such as CT and PET/CT. The information and images will be labeled with a study-specific code and a code number called a Global Unique Identifier (GUID), which is a computer-generated code that is unique to each research participant through software provided by the National Institute of Health (NIH). A confidential list of names will link the code to your name. Only authorized personnel (for example, the study doctor) will have access to the list of names and be able to identify you.

The GUID enables researchers to see if patients enroll in multiple studies, because you would receive the same code for each study that employs the GUID coding system. Therefore, the data from this study could be used in unspecified, future research that is similar in nature to what is being done with this study.

The study doctor will keep your medical records and any other record identifying you confidential. To the extent permitted by law, monitors, auditors, the FDA, the Institutional Review Board (IRB) and other competent authorities will have access to your medical records in order to verify the

study data and compliance with the study procedures. Those persons will have the obligation to keep your records and the information contained in them confidential.

Study records that identify you will be kept confidential as required by law. The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your protected health information (PHI). The document you are reading, called an "**Authorization**," explains how your PHI will be used and disclosed (shared) for purposes of the research study and describes your rights with respect to such information.

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. Confidentiality of your records will be maintained to the extent possible. However, the Health Authorities, the Monitors and other study personnel representing the Sponsor, the IRBs, Ethics Committees and regulatory authorities and your health insurance company may need and will be granted direct access to your medical records to verify either the procedures or the data they contain. By signing this consent form you are giving your authorization for such access. This consent form will be kept in a research file that is separate from your medical records.

Results of laboratory tests and clinical procedures will be placed in your medical record and may be accessible to employees of the health system that are not part of the research team. However, your medical records will not hold any individual genetic results.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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.

What information about me may be collected, used, or shared with others?

If you choose to be in this study, the study doctor will collect personal information from you. This information may include:

- Medical and Research Records
- Name, address, telephone number, medical record number
- Date of birth
- Social Security Number for reimbursement purposes, if required
- Email Address
- Records about study-related phone calls
- Records about your study visits
- Records of physical exams, tests and procedures
- Laboratory and other test results
- Records about study drugs

- Any medications that you are taking
- All of your current and past medical history

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- see if the research was done right
- to evaluate and manage research functions

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at the University of Pennsylvania, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of the School of Medicine, might receive my information?

All research centers participating in the study, even if they are not part of the School of Medicine, might receive your information.

If you have blood tests done for research at a blood draw facility near you, such as Quest Diagnostics or LabCorp, the facility will receive your information, including test results.

Pfizer, the company that is supplying the study drug, may receive information about adverse events.

A travel service may receive information about you so that travel arrangements can be made.

<u>Oversight organizations</u>

- The FDA
- The Office of Human Research Protections
- The Institutional Review Board
- The study DSMB

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's IRB grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

If you withdraw from the study and withdraw your authorization, no new information will be collected for study purposes unless the information concerns a side effect related to the study. If a side effect occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about a side effect related to the study, will be sent to the study sponsor. If you withdraw from the study but do not withdraw your authorization, new PHI may be collected until this study ends.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Subject Informed Consent Form and HIPAA Authorization describing your confidentiality and privacy rights for this study. By signing this document, you are permitting School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

You do not have to sign this Authorization, but if you do not, you cannot participate in this research study or receive study-related treatment. If you withdraw your authorization in the future, you will no longer be able to participate in this study. Your decision to withdraw your authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).

Care Everywhere and Research: Care Everywhere is a functionality that exists between Penn Medicine and the Electronic Medical Record (EMR) system called EPIC. It allows other health care facilities outside of UPHS to share patient data within EPIC to improve patient care. Researchers may also use Care Everywhere to view health information as it pertains to research.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form.

If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this consent form and authorization, you are agreeing to take part in this research study. This means that you have read this consent form and authorization, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A signed and dated copy of this consent form will be given to you.

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

_____	_____	
Authorized subject representative **[print]**	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.

_____

SUPPLEMENTAL INFORMED CONSENT DOCUMENTATION

Risks and Benefits of Investigational Product

This document is to be used prior to administration of investigational product if informed consent was initially obtained by a designee who is not a Pennsylvania-licensed physician.

A licensed physician has explained the portions of this Informed Consent Form relating to the risks and benefits of the investigational product.

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date

_____	_____	
Name of Physician Obtaining Consent (Please Print)	Signature of Physician	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

_____	_____	
Authorized subject representative **[print]**	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.

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