UPMC LIFE CHANGING MEDICINE

INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

FOR SUBJECT PARTICIPATION IN A RESEARCH STUDY / Recipient Informed Consent

TITLE OF CLINICAL TRIAL: Safety and Preliminary Efficacy of Donor-derived Regulatory Dendritic Cell (DCreg) Infusion and Immunosuppression Withdrawal in Living Donor Liver Transplant (LDLT) Recipients

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QUESTIONS ABOUT THE STUDY:
You can contact the study investigator if you have any questions about the study, concerns or complaints. Contact one of the investigators listed above at 412-647-5800 (24 hours)

If you have any questions about your rights as a research subject or wish to talk to someone other than the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

SOURCE OF SUPPORT: University of Pittsburgh Medical Center

INTRODUCTION:
You are invited to take part in this research study for adults between the ages of 18 and 75 who are scheduled to receive a living donor liver transplant and whose care will be managed at the University of Pittsburgh Medical Center (UPMC). Before you can decide whether or not to take part in this study, we would like to explain why the study is being done, what will be expected of you, and the possible risks, benefits, and alternatives to participating in this study.

Your physician is involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

People who have liver transplants must take anti-rejection medication (immunosuppression) for the rest of their lives. If they stop immunosuppressive medications, their immune system may reject the transplanted liver. All anti-rejection medications have side effects. Anti-rejection medications make it hard for your body to fight off infections. In addition, they can cause high blood pressure, kidney damage, and plaque build-up in the blood vessels, high cholesterol, diabetes, and bone disease. They may also make you more likely to get some types of cancer (mainly cancer of the white blood cells and/or skin) and other serious side effects.

In this study, our goal is to develop a new, safe treatment approach that involves injecting immune cells called regulatory dendritic cells (DCreg) from the transplant donor into the transplant recipient prior to the liver transplantation. We expect that this will make your body more accepting of, or tolerant, to the transplanted organ and facilitate the withdrawal of immunosuppressive medications without jeopardizing the function of the transplanted organ.

Your anti-rejection medication(s) will be gradually reduced over a period of time and then completely stopped. The study calls this 'immunosuppression withdrawal'. In previous research studies, about 15% of the participants are able to stop their anti-rejection medication(s) completely without experiencing organ rejection.

The purpose of this research is to study if donor DCregs are safe to be injected into recipients, like yourself, and to see how many of these recipients will develop tolerance after withdrawal of immunosuppressive medications.

RESEARCH ACTIVITIES

This study is sponsored by the UPMC. The study will be conducted at UPMC Presbyterian and Montefiore location. The study will enroll up to 15 living donor liver transplant recipients and their living donors.

Total duration of subject participation in the study is approximately 4.5 years.

If you agree to participate the study will consist of the following:

Your liver donor will be approached and asked to undergo a procedure called leukapheresis (similar to plasma donation) several weeks prior to your transplant surgery. If they agree they will be given a separate informed consent to sign for this study. During the leukapheresis procedure, white blood cells called monocytes will be taken out of their blood, and other parts of their blood will be returned to their body. In a laboratory, we will prepare DCregs from these monocytes.

You, the transplant recipient, will then receive a single infusion of donor-derived DCreg, 7 days prior to the transplantation, followed by weaning of immunosuppressive medication beginning at approximately one year post-transplantation. Weaning is expected to last up to about one year.

Samples (blood, urine, and liver tissue) are collected during the study. These samples are used for research tests. Research tests help us learn more about your disease, the immune system, and liver transplantation. The results of the research tests will not be shared with you.

Research tests may include genetic tests. These laboratory tests study your inherited (present from birth) characteristics, which are present in each of your cells. Genetic tests study an individual's inherited characteristics, found in DNA, which is present in each of the cells of your body. DNA contains information needed to construct and operate a human body. Genetic testing may help researchers learn more about your disease or help to find treatments for your disease. As with all research tests, these

results will not be shared with you unless they are also part of your routine clinical care.

You will be asked to complete a written survey called the SF-36 "Quality of Life" survey at approximately 1 year after your transplant and at the end of the study.

Your medical record information will be accessed and collected as it relates to your participation in this study. We will obtain the following information: your diagnosis, age, past medical history, diagnostic procedures, and results of any tissue biopsies or blood tests, including routine tests that were already done as part of your standard evaluation at the Starzl Transplantation Institute.

SCREENING:
You have undergone rigorous screening as part of standard of care prior to being deemed eligible for a living-donor transplant. Therefore, a separate screening visit specifically for the purposes of this study will not typically be needed.

The visit schedule for the DCreg infusion and pre-immunosuppression withdrawal is shown in the Table below:

Visit Schedule for DCreg Infusion and CONCURRENT IMMUNOSUPPRESSION (IS)										
Visit Schedule	1	2	3	4	5	6	7	8	9	10
Days	-28d to-7d	-7d	-3d to-1d	0 (surgery)	10d	14d	28d	60d	90d	120d
DCreg infusion		X								
Liver Tissue and Lymph Node Collection for Research				X						
Physical Exam/ Vital Signs	Collected from Routine Clinical Care Visits at approximately days 1, 7, 14, 30 and at approximately months 3, 6, 9 post-transplant.									
Blood collection for clinical Care (~ 2-3 tsp)	Collected from Routine Clinical Care Visits at approximately days 1, 7, 14, 30 and at approximately months 3, 6, 9 post-transplant.									
Tacrolimus Trough Levels	Collect from Routine Clinical Care									
Blood Collection for Research (~ 7 tbsp)		X					X		X	
Blood Collection for Research (~ 1 tbsp)			X	X						
Spot Urine collection for Research							X		X	

DCreg INFUSION:
Before the DCreg infusion you will be given specific instructions from your study coordinator.
You will undergo an approximate 4 – 6-hour outpatient DCreg infusion visit at the 7 West Starzl Transplant Outpatient Center or the Clinical and Translational Research Center (CTRC) at UPMC Montefiore Hospital.

Upon admission to 7 West Transplant Outpatient Center or the CTRC, you will undergo a physical examination and a peripheral venous line (catheter into vein) will be inserted in your arm.

The DCregs are prepared from certain blood cells called the monocytes. The lab can estimate the number of DCreg cells from the number of monocytes collected during the donor's leukapheresis procedure. We will not know the exact number of DCreg cells manufactured until the day of infusion. In the unlikely event that the exact dose of the DCreg cells is too low, you will not receive the DCreg infusion and the cells will be discarded.

In the morning, prior to DCreg infusion, you will take an immunosuppression medication, MPA (mycophenolic acid). Typically, this will be given as a 500mg dose of a medication called mycophenolicate mofetil (MMF; CellCept®). It is possible that you will be given and equivalent dose of enteric coated Myfortic®. From this day until the day of transplant, you will continue to receive MMF 500mg twice daily (1/2 of a standard dose you will receive after transplantation) or equivalent dose of Myfortic® to minimize the low potential risk of sensitization caused by the infusion of donor-derived DCreg. You will be provided a bottle with a 7-day supply of MMF or MPA and will be asked to return empty bottle when they come in on day of transplant.

You will then have a 12-lead EKG (test used to measure the electrical activity of your heart). Prior to the infusion of the DCregs, you will have a cardiac (heart) monitor placed, which will be continuously monitored throughout the infusion and for one hour after the infusion.

Vital signs (temperature, blood pressure, respirations, pulse, pulse oximetry) will be checked at baseline (prior to transfusion), every 15 minutes during the infusion and for one hour after completion of infusion. Vital signs will then be monitored every 30 minutes for the next three hours for a total of 4 hours of monitoring after completion of infusion.

To ensure your safety approximately ½ tbsp of blood will collected for routine blood work prior to your infusion and at about one hour after the infusion.

For research, we will collect approximately 7 tbsp of blood prior to the DCreg infusion and then about 1 tbsp of blood within approximately 1 hour after the infusion.

Thirty to sixty minutes before the DCreg infusion, you will receive a dose of acetaminophen (such as Tylenol) 500mg-1000mg by mouth to reduce the chance of a fever from the infusion. Additionally, you will also receive a dose of diphenhydramine (such as Benadryl) 25-50mg by mouth or through the catheter in your vein to reduce the chance of developing hives or itching. The DCreg infusion will be given to you in the form of a solution that will be administered into your vein by hospital staff and will take approximately 60 minutes. After the infusion is completed, a 50ml normal saline (salt) solution will be administered over about15 minutes.

During the entire time you are on 7 West or CTRC, study team members (including a doctor and nurse) will be present or immediately available for any questions or complications that may arise. You will not be discharged from 7 West or CTRC until post-infusion blood test results have been reviewed and the study team determines that it is safe for you to leave. Prior to leaving the 7 West or CTRC, you will be given instructions and contact information to call if you have any questions or concerns after your treatment.

1 to 3 Days Prior to Transplant Surgery:
Approximately ½ tbsp of blood will be collected for research purposes.

Day of Transplant Surgery:
Prior to your Liver Transplant surgery, we will collect approximately 1 tbsp of blood for research.

Liver Tissue and Lymph Node Collection for Research:
At the time of your transplant surgery, after your old liver has been removed along with some lymph nodes, we will take pieces of the liver and lymph nodes for research. Since we are obtaining these samples after your old liver is removed, there is no added risk to you. If no lymph nodes are removed with your old liver the transplant surgeon will collect up to 4 lymph nodes from your abdomen to be given to the research team.

During your surgery, your transplant surgeon may take a liver biopsy (a small piece) of your new liver. This will be taken within approximately 60 minutes following the restoration of blood flow to your newly transplanted liver. This will be used as a baseline reading.

The Immunosuppression Weaning visit schedule is shown in the Table below:

Visit Schedule: Immunosuppression (IS) Weaning		
	MMF/MPA Wean (regular clinical care)	Prograf Wean
Visit Schedule	11	12
Months	by 12m	12m
Routine Clinical Care Liver Biopsy		X
Physical Exam/ Vital Signs	Collected from Routine Clinical Care Visits at approximately 12 months post-transplant.	
Blood collection for clinical Care (~ 2-3 tsp)	Collected from Routine Clinical Care Visits at approximately 12 months post-transplant.	
Tacrolimus Trough Levels	Collect from Routine Clinical Care	
Blood collection for research (~ 6 tbsp)	X	X
Spot Urine collection for research	X	X
Quality of Life Survey (QOL) Survey		X
Telephone Consult	Every time liver tests are collected at subject's local lab/clinic and prior to new immunosuppression taper level	

Immunosuppression Weaning Phase
As part of your routine clinical care by 6 months post-transplant if you have not experienced any of the following:

i. Rejection episode(s)
ii. Abnormal blood work

then you will begin the first phase of immunosuppression weaning (MMF wean).
At 12 months post-transplant if you have not experienced any of the following:

i. Rejection episode(s),

ii. Abnormal blood work,
iii. Abnormal 12 month routine biopsy,

then you will qualify to proceed with the second phase of the study (Prograf Weaning).
During the Prograf Withdrawal phase, your dose of anti-rejection medication(s) will be slowly reduced. The research staff will tell you when and how to do this. It will take up to about one year to completely stop your anti-rejection medication(s). If we did not infuse the donor DCregs into your body prior to transplantation you would have about a 15% chance of completing the withdrawal process without experiencing rejection of your transplanted organ. We are conducting this study to see if the DCregs improve those chances. If you do experience rejection, your physician will treat you for rejection as he/she thinks best. In almost all cases, rejection that occurs during drug withdrawal is easily treated, without any lasting effects. It is possible; however, after treatment for rejection you will be taking more anti-rejection medicine than previously. It is also possible that you could experience an episode of rejection that is difficult to treat, or that cannot be treated successfully.

Patients who fail eligibility for weaning will return to routine clinical care and will be followed up for the rest of the duration of the study.

Rejection during Prograf Immunosuppression Weaning
Lowering your dose of anti-rejection medication might increase your risk of acute rejection. Acute rejection happens when your immune system causes damage to the transplanted liver.
If you experience rejection during withdrawal:

- You will receive treatment. The study doctor will determine how your rejection is treated and what medications to use.
- A 'for-cause' biopsy will be done. During your liver biopsy two biopsy samples will be collected. One for clinical care and one for research.
- About 3 tbsp of blood will be collected for research at the time of the biopsy. Urine will also be collected for research.
- You will have weekly liver blood tests until the rejection has ended.
- Patients, who fail weaning for any reasons, will return to routine clinical care and will be followed up for the rest of the duration of the study.

FOLLOW-UP PHASE:
You will be followed approximately 4.5 years total for the study, regardless of whether you can complete immunosuppression withdrawal or not.

If you fail the immunosuppression withdrawal phase, the follow up procedures include those of your routine, standard of care treatment. You will be instructed by your clinical coordinator at the Starzl Transplant Institute on how often you should return to see the doctor and how often you should have blood work drawn to monitor the function of your liver. For the purposes of the study, these data will be collected to monitor study safety and whether or not the DCreg infusion was beneficial to your overall heal

The Follow-Up Phase Visit Schedule is shown in the table below:

Visit Schedule 3 year follow-up							
Visit Schedule	13	14	15	16	17	18	19
Months	18m	24m	30m	36m	42m	48m	54m

Routine Clinical care Liver Biopsy			X				
Research Liver Biopsy							X
Physical Exam/ Vital Signs	Per Standard of Care						
Tacrolimus Trough Levels	Collected every 2 weeks until level undetectable after weaning						
Blood collection for clinical care (~ 2-3 tsp)	Every 2 weeks		Monthly				
Blood collection for research (~ 6 tbsp)	X		X				X
Telephone Consult	Every time liver tests are collected at subject's local lab/clinic and prior to new immunosuppression taper level						
Spot Urine collection for research		X		X		X	
Quality of Life Survey (QOL) Survey							X

The total amount of blood drawn during your participation in the study will be about 180 tbsp or about 12 cups.

STUDY RISKS:
As with any experimental procedure, there may be adverse events or side effects that are currently unknown, and certain of these unknown risks could be permanent, severe or life-threatening. Treatment and procedures in this research study may involve risks that are not possible to predict. You will be informed of any new risks that may be identified during the study. Please ask your study doctor or the research staff to explain any procedures or risks that you do not understand. You might have more problems as a result of participating in this research study than you would have if you continued routine treatment. These unknown risks may affect you during your participation in the research study and/or at some point in the future.

Risk of DCreg infusion:
This study is the first time that donor DCregs will be infused into human liver transplant recipients. Extensive animal studies have shown no adverse effects on the recipient animals; however, we know from studies of other cell types that when recipients are exposed to donor cells, sensitization (a reaction against the transplanted organ) may occur. Throughout the study we will monitor you for this. Sensitization does not make potential liver recipients ineligible for transplantation.

The following side effects could potentially occur, but we expect them to be very rare: allograft rejection secondary to sensitization, graft loss due to rejection, an infection as a result of having your immune system suppressed and not specific to the donor cells that you receive from the infusion, and malignancy secondary to immunosuppression and not specific to the donor cells you receive from the infusion, and patient death.

Anytime something is infused into a blood vessel the following side effects may occur: pain, redness, bleeding and swelling at site of injection; fever, headache, infection, cell embolism (a blood clot), and

allergic reactions such as rash or bronchospasm (difficulty breathing).

During the infusion, there is also a risk of cytokine release syndrome. This syndrome can sometimes occur after therapeutic infusion of immune cells into the blood and is characterized by nausea, headache, tachycardia, hypotension, rash, and shortness of breath. It is caused by the release of cytokines (small protein released by cells) from the cells. Because the cells that we are infusing are not activated and are not expected to activate the immune cells in your body, we expect this to be a rare event resulting in a mild to moderate reaction. However, it is possible for cytokine release syndrome to be severe and life-threatening.

During the infusion, the study team may give you medicines to help reduce some side effects that you may experience. The study team may also temporarily or permanently stop the DCreg infusion without your agreement for your safety

Risk of Withdrawal of Immunosuppression: Rejection

Risk of Chronic Rejection:
There is a small chance (<2%) of developing chronic rejection. Chronic rejection is harder to treat than acute rejection but with the many medications available today, it is likely that chronic rejection can be reversed. If the treatment for chronic rejection does not work, the liver could fail. If the liver fails, another liver transplant may be needed in order to live. It is possible that you could die while waiting for another liver transplant. If the treatment for chronic rejection works, your liver can fully recover from chronic rejection.

Rejection:
The most serious risk is rejection of transplanted liver. Rejection can occur at any point during the study. You may not be able to continue to reduce your immunosuppression as part of this study after you've had rejection or been treated for rejection. If your liver tests increase, whether or not you are in the Immunosuppression Withdrawal phase, additional liver tests and / or a liver biopsy may need to be done (see risk of liver biopsy, below). The medications used to treat rejection have additional risks and side effects.

It is very likely that treatment will end an acute rejection episode. The liver can fully recover from rejection, without long-term consequences. The chance that an acute rejection episode is either difficult to treat or cannot be treated is low, estimated at <1.0%.

Risks of Treatment for Rejection:
Treatment for rejection usually requires increase in immunosuppressive medications over and above what you were taking at the time of rejection. It is possible that treatment of rejection might require, at least for some time, more immunosuppression than your starting dose at the beginning of the trial. If you suffer acute rejection or chronic rejection, you might need more immunosuppression for some time. Taking more immunosuppression can increase chances of infection and other side effects of anti-rejection medications such as diabetes, high cholesterol, and cancer. Also, depending on the medications used to treat rejection, you might be put on extra medications that you will need to take for several months to prevent specific infections. The study doctors will tell you about the side effects of these medications.

Risks of Liver Biopsy:
In this study, you will have more liver biopsies than if you were not participating in an experimental study, even if your liver function is fine. Most transplant patients undergo a biopsy of their transplanted liver at about one year and two and a half years post liver transplant and if otherwise clinically indicated. They would also have a biopsy when there could be a problem with their liver function. **For all liver**

biopsies performed during the study two biopsy samples will be collected. One sample will be read by the pathologist and the second sample will be saved and stored for research purposes. All liver biopsies will be performed by a trained medical professional at UPMC.

These biopsies will inform your physician of the condition of your liver as well as help investigate the presence and location of infused DCreg. **Except for the biopsies collected while you are asleep in the operating room you will sign a separate consent form when you have each liver biopsy**. This consent form will explain details of the biopsy procedure, any medications you will receive before and during the biopsy, and any risks associated with the biopsy.

As with all the procedures, your study doctor will do all that is possible to avoid these risks; however, some risks may require medical or surgical care after the biopsy. The risk of death from liver biopsy is extremely low, ranging from 0.1% to 0.01%. The most frequent problem from a liver biopsy is bleeding. The risk of bleeding ranges from 0.35% to 0.5%.
The risk of liver biopsy includes:

- Bleeding
- Low blood pressure
- Shoulder pain
- Pain at the needle insertion site
- Accidental puncture of other organs (lung, kidney colon and gallbladder)
- Infection

Risk of Lymph Node removal:
As with all the procedures, your study doctor will do all that is possible to avoid these risks; however, some risks may require medical or surgical care after the biopsy.
The risk of lymph node removal includes:

- Bleeding
- Infection
- Tissue/ Organ Injury: Although uncommon, adjacent organs and tissues may be injured as a result of your surgery. This includes kidneys, colon, bowel, vascular structures, nerves, muscles, lungs, spleen, liver, pancreas and gallbladder. On rare occasions, further surgery may be required to address these unexpected injuries.
- Lymphocele: Lymphatic fluid can rarely collect in the area where the lymph nodes were removed, which may require drainage of the fluid or further surgery.

An on-call transplant pathologist will be in the operating room to examine the lymph nodes for any cancerous tumors prior to providing them to the research team.

Risk of Blood Draw:
The risks of having blood taken are discomfort, bleeding, fainting, small blood clot or swelling to the vein and area surrounding where the blood is drawn, bruising where the needle enters the skin and infection. There is also a very small chance of infection at the needle puncture site.

Risk of EKG/ Cardiac Heart Monitor:
Sometimes the adhesive pads used to attach the leads (plugs) for recording the activity of your heart (EKG) can cause skin irritation which also clears up after a while.

Risk of Survey:
There is a risk that you may feel a particular question on the surveys is too sensitive to answer. It is OK to skip a question that you feel uncomfortable answering.

Risk of Breach of Confidentiality:
Although every effort is made to protect your confidentiality, there is a risk that someone else may inadvertently see your private health information

Risk of Acetaminophen:
Acetaminophen is considered to be safe and effective in the recommended doses, according to the 'Drug Facts' label. When taken incorrectly, however, acetaminophen can cause liver damage. And your risk of liver damage may be increased if you drink more than three alcoholic drinks every day, take more than the recommended dose (overdose), or if you take any additional drugs that also contain acetaminophen at the same time

Risk of Diphenhydramine (Benadryl):
Common side effects of Benadryl include sedation, tiredness, sleepiness, dizziness, disturbed coordination, constipation, dry mouth/nose/throat, difficulty urinating, and upset stomach. Benadryl may also cause headache, blurred vision, double vision, tremor, loss of appetite, dry mouth, or nausea.

Risks of Normal Saline Flush:
Common side effects of Normal Saline include fever, injection site swelling, redness, or infection. Uncommon but serious side effects of Normal Saline include fast heartbeat, fever, rash, joint pain, or shortness of breath.

Risk of Mycophenolate Mofetil (MMF):
Common side-effects are diarrhea, vomiting, and decrease in the number of red and/or white blood cell. Rarely, you may experience gastrointestinal bleeding. Cases of progressive multifocal leukoencephalopathy, a rare, often fatal, infection of the brain have been reported in people taking MMF.

Risk of Mycophenolic Acid (MPA):
Common side-effects are constipation, diarrhea, nausea, vomiting, and decrease in the number of red and/or white blood cell. Rarely, you may experience gastrointestinal bleeding.

Risk of Genetic Testing:
The risks associated with genetic studies include the potential for a breach of confidentiality which could affect future insurability, employability, or reproduction plans, or have a negative impact on family relationships and/or result in paternity suits or stigmatization.

STORING INFORMATION FOR FUTURE STUDIES:
We will store information from this study, including genetic information, in a central Data Repository/Archive. The purpose of this is to make data (including information resulting from testing DNA) available for use in health research. Any information released to a central data repository will not contain your personal information.

A central data repository is a research resource. It collects, stores, and distributes information from many different people. The purpose of this collection is to make scientific information available for future studies which may help future patients. Your data may be stored indefinitely and will not reveal your identity.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information that we get from this research when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

STUDY BENEFITS:
If you agree to take part in this study there may be no direct medical benefit to you. If you successfully stop taking anti-rejection medications, you might benefit by not experiencing some of the common side effects of anti-rejection medications such as infection, kidney problems, diabetes and cancer. The information gathered during this study may someday be of benefit to future liver transplant recipients.

ALTERNATIVE TREATMENTS:
Before you decide to take part in this study, one of the investigators listed on the first page will talk with you about these and other options available to you. If you choose not to participate in this study, you will not receive the DCreg infusion and will be treated with standard anti-rejection medication(s).

NEW INFORMATION:
You will be promptly notified if any new information we learn during this research study may cause you to change your mind about continuing to participate in the study.

PRIVACY (Person) and CONFIDENTIALITY (Data):
Your personal details and information from the study are processed in accordance with United States data protection law, the Health Insurance Portability and Accountability Act (HIPAA), which is designed to protect your privacy. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality due to the nature of the data being collected, which includes genetics and private health information.

Why is this information needed?
This information is needed to determine whether you meet the conditions for participation in this study, to compare your earlier test results to the findings from this study, and if possible, to use your previous exam results in place of, or in addition to, some of the exams needed for this study.

You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study. After the study is completed, the data may be placed in a central storage location. These data will not include your name or other information that can identify you. The purpose is to make study data available to other researchers.

Your research data/samples and genetic data generated from samples may be shared with investigators and with federal repositories conducting other research; this information will be shared without identifiable information. These research data/samples may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development

of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

What will be disclosed?
We will obtain the following information: your diagnosis, age, past medical history, diagnostic procedures, and results of any tissue biopsies or blood tests, including routine tests that were already done as part of your standard evaluation at the Starzl Transplantation Institute.

Who is requesting the Protected Health Information (PHI) for research?
In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:
Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this study.

Authorized representatives of UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders made by the investigators for hospital and health care services (e.g. laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).
Authorized representatives from the U.S. Food and Drug Administration (FDA) may review and or obtain your identifiable (which may include your identifiable medical information) related to your participation in this research study for the purposes of monitoring the accuracy and completeness of the research data. While the FDA understands the importance of maintaining the confidentiality of your identifiable research and medical information, the UPMC and University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the FDA.

UPMC its designee(s), its collaborator, auditors, monitors, ethics committee, independent review boards and various government health agencies (such as the FDA) in this or other countries will have access to your records and data collected and may inspect and/or copy your medical records of this study. You also provide consent for the release of copies of your laboratory test results and medical reports for review as part of this research study. Information about your disease status may be requested and reviewed on a regular basis after you have completed all visits in this study. This is necessary to ensure that the study is performed according to the approved protocol, for participants' safety, and that the data collected is correctly recorded.

There are national and state laws that make the study doctor protect the privacy of your records. However, you do not have a guarantee of absolute privacy because of the need to share your information. After the study doctor shares your records with UPMC and others, the laws may no longer protect the privacy of your records. UPMC or others may share your records with other people who do not have to protect the privacy of your records.

How long will this information be made available to the researchers?
The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for a minimum of 7 years and for as long (indefinite) as it may take to complete this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with who you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

We will protect your privacy and confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records, once your personal information is disclosed to others outside UPMC or the University.

Do I have a right to revoke this authorization?
You always have a right to withdraw your authorization to allow the research team to review your medical records by contacting the investigator listed on the first page and making the request in writing. 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 this 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.

How long will this authorization be valid?
This authorization is valid for an indefinite period of time.

FDA CLINICAL TRIAL REGISTRY:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WITHDRAWAL FROM STUDY PARTICIPATION:
You can, at any time withdraw from this research study; you can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.
If you decide to withdraw from study participation after, you should participate in additional monitoring follow-up procedures that are being conducted to measure the safety of the study.

If you withdraw your consent:
-You will not be able to continue in the study
-The study doctor will not be able to use or share any future health information unless it is necessary to protect the integrity of the study. The data collected before your withdrawal remains part of the study database and may not be removed.
Even if you leave the study early, the study doctor or study staff will still be able to use and share your records as described above unless you withdraw your consent to use and share your records.

It is possible that you may be removed from the research study by the researchers if, for example,
- If you do not follow your study doctor's instructions
- If your study doctor feels it is necessary for your health and safety

- Pregnancy
- If we find out you should not be in the study
- If the study is stopped or cancelled
- Unanticipated circumstances
- If you are unable to receive DCreg Infusion for your health and safety

If your study doctor decides that you should withdraw from the study due to any of the above reasons, you will be followed with additional monitoring to measure the safety of the study. The monitoring follow-up procedures are that of your standard of care treatment. You will be instructed by your clinical coordinator at the Starzl Transplant Institute on how often you should return to see the doctor and how often you should have blood work drawn to monitor the function of your liver. The study team will collect data from any laboratory results, doctor visits, and imaging tests from these routine follow-up procedures until the end of your study schedule is reached.

COSTS:
While you are in this study, you still need to receive regular medical care. You or your insurance carrier will still have to pay for the costs of your regular medical care that are not part of this study. These include cost of clinic/doctor visits, lab and radiology procedures that are not part of the study. You are encouraged to speak with your insurance company about what will be covered before agreeing to take part in this study.
UPMC will cover the costs of the tests that are done specifically for this study (for example, the DCreg infusion and blood tests) and provide the study agent to you at no charge. Your health plan/insurance may pay for all tests and procedures that would normally be done as standard of care; that is, those procedures or tests that you would normally have as part of your regular medical care.

PAYMENTS:
We will reimburse you for certain study-related expenses such as travel or parking costs to attend in-person study visits.

We will compensate you for time spent at study visits that do not coincide with standard of care. Since the DCreg infusion visit will be several hours long, we will pay you $80 for that visit. For shorter research-only visits, such as research blood draws, we will pay you $20.00. You may choose to have all, some or none of your research blood draws at Quest Diagnostics. If you go to Quest for your research blood draw, or if the results of your standard of care blood tests can be used, you will not receive any payment. You will receive all payments at the end of each research visit for your participation in this study.

COMPENSATION FOR INJURY:
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not, however, waive any legal rights by signing this form.

VOLUNTARY PARTICIPATION:
Your participation in this research study is entirely voluntary. You may want to discuss this study with your family and friends and your personal physician before agreeing to participate. If there are any words you do not understand, feel free to ask us. The investigators will be available to answer your current and future questions.

Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

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CONSENT TO PARTICIPATE:
The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given.

I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the Human Research Protection Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Printed Name	Participant's Signature	Date and Time

INVESTIGATOR CERTIFICATION:

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date and Time