Title of research study: ***Personalized Infliximab Induction Strategy with Model-informed dosing in Patients with Crohn's Disease (REMODEL)***

Key Information:

The following is a short summary of this study to help you decide whether to be a participant in it. More detailed information about the study is listed later in this form. This document does not replace the discussion you should have with the research team about this study including having any questions or concerns answered.

If you are 18 years and older: This is a consent form. It explains this research study. If you decide that you want to be in this research study, then you will sign this form to show that you agree to be part of this study. If you sign this form, you will receive a signed copy of it for your records.

Parental Permission: If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required using a separate form. When we say "you" in this form, we mean you or your child; "we" means the study doctor and other staff.

Investigator:
Phillip Minar, MD, MS

Contact Info:
513-636-4415

Industry Protocol #:
REMODEL

Drug Name:

Infliximab

Funding:

Crohn's and Colitis Foundation

Cincinnati Children's Research Foundation (ARC)

Reason for the study:

Approximately 3 million people in the United States are living with inflammatory bowel disease, which includes Crohn's Disease, with many of those being young children and adolescents. We need better ways to inform decisions on treatment.

We are asking you to be part of this research study because you have been diagnosed with Crohn's Disease and you are going to start treatment with infliximab as part of your routine clinical care.

Infliximab is a FDA-approved drug to treat Crohn's Disease. Currently, dosing of infliximab is based only on your weight. However, this method of dosing may increase the risk of low levels of infliximab in your blood and result in poor control of your Crohn's Disease.

The main reason for this research study is to determine if a computer program that formulates a dose based on your blood testing results can better achieve the optimal drug level as compared to standard dosing.

For this study, we will enroll 20 people between 6 and 22 years old with Crohn's Disease.

Procedures:

The following tests and procedures will take place if you decide to participate in the research study.

- Information will be collected from your medical records.
- You will be asked to complete questionnaires several times.
- You will have blood samples taken in connection to receiving your medication.
- You will provide stool samples.
- You may have urine collected for a pregnancy test.
- You may choose to have an MRI.
- Guided by the computer program dosing recommendation, your doctor will decide the starting infliximab dose as well as subsequent doses and the amount of time between doses.

We expect that you will be in this research study for 6 months.

More detailed information about the study procedures can be found under ***"(Detailed Procedures)"***

Risks to Participate:

The drug used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood, possibly causing side effects. The table below shows the most common and most serious side effects that researchers know about. We do not know all of the side effects that may occur.

COMMON, SOME MAY BE SERIOUS	
• Allergic reaction	Seen in at least 5 out of 100 people
• Serious Infection	Seen in at least 3 out of 100 people

More detailed information about the risks of this study can be found under ***"(Detailed Risks)"***

Benefits to Participate:

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include improved control of your Crohn's Disease and improved drug durability (longer time on the drug). This study will provide invaluable data regarding future treatment plans for dosing of infliximab.

Other Options:

Participation in research is completely voluntary. Your decision to participate or not to participate will not affect the care you receive.

Your alternative to participating in this research study is to not participate.

Cost to Participate:

You and your insurance company will be charged for the healthcare services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Payment:

If you agree to take part in this research study, we will pay you $15 for each laboratory (blood) and survey collection and $25 for each stool sample provided (up to 4 times). We will also pay you $25 for Visit 2 (optional blood collection) and $75 for Visit 8 (optional MRI). You (your child) will receive payment for this study in the form of a reloadable debit card (ClinCard). We will give you (your child) a handout that will explain how to use the card. Because you (your child) are being paid for your participation, Cincinnati Children's is required by the Internal Revenue Service (IRS) to collect and use your (your child's) social security number (SSN) or taxpayer identification number (TIN) to track the amount of money that we pay. You will need to complete a Federal W-9 form for this income tax reporting. This form requires your child's Social Security number. This form will be given to the Cincinnati Children's business office. It will not be kept as part of your child's study chart. If you move, you will need to complete another W-9 with an updated address.

Additional Study Information:

The following is more detailed information about this study in addition to the Key Information.

If I have Questions or would like to know about:

Who to talk to…	**You can call …**	**At …**
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**PI Name: Phillip Minar, MD, MS**	Phone: 513-636-4415

Who to talk to…	You can call …	At …
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**Lead Study Coordinator: Kimberly Jackson**	Phone: 513-803-4181
• Your rights as a research participant	**Institutional Review Board** This is a group of scientists and community members who make sure research meets legal and ethical standards.	Phone: (513) 636-8039

Detailed Procedures:

- Consent- You will need to read and sign this consent form before doing any study procedures. You will get a copy to keep.
- You will have approximately 20 ml (4 teaspoons) of blood collected prior to each infusion and at visit 2. In addition, about 6 ml (1 teaspoon) of blood will be collected after infusions 1, 2, 3, 4, and 6.
- You will interact with the study doctor and the study staff. The study staff will contact you prior to visits as a reminder of upcoming visits and stool samples.
- Questionnaire- You will answer some questions about your stomach pain, stool frequency, and general well-being.
- Medical Record Review- Study team will review your medical records for information on your health, medical history, and current medications.
- Physical Exam- The clinician will examine your temperature, heart rate, breathing rate, blood pressure, height, weight and an abdomen examination.
- Pregnancy Test- If you are female, we will ask you to give a small sample of urine for a pregnancy test. If it is positive, you will not be allowed in the study.
- Stool Collection- You will be asked to collect stool at home and either mail the samples or bring them to your infusion visits. You will be provided the kits for collection and mailing.
- Drug Infusion (first 3 doses) - As part of your normal infusion visits, you will receive infliximab at 0, 2, and 6 weeks.

- Drug infusion (doses 4, 5, and 6) - As part of your normal infusion visits, you will receive infliximab every 4-8 weeks. The dosing schedule is variable and is informed by the computer program and your doctor.
- Your infusions will need to take place at Cincinnati Children's while you are in the study.
- MRI- You will have the option to obtain an MRI scan. This will occur at visit 8 and is optional.
- You may be contacted for future research.

Procedures	Screen	V1	V2	V3	V4	V5	V6	V7	V8
Timeline (infusion)		**1**		**2**	**3**	**4**	**5**	**6**	
Weeks (range)		**0**	**1**	**2**	**2-6**	**10-14**	**14-22**	**18-30**	**26-30**
Ensure you qualify to participate in this study	X								
Collect Demographic information	X	X							
Collect Medical History	X							X	
Collect Surgical History	X							X	
Perform Physical exam	X							X	
Record Clinical Lab Results	X	X		X	X	X	X	X	
Ask about current and past medications	X	X		X	X	X	X	X	
Perform urine pregnancy test (female participants)	X								
Complete GI Symptoms Questionnaire	X	X	X	X	X	X	X	X	
Receive infliximab infusion		X		X	X	X	X	X	
Collect blood sample(s)[1]		X	X	X	X	X	X	X	
Collect Stool samples[2]		X			X	X		X	
Study staff phone calls[3]		X				X		X	
Perform Optional MRI abdomen [4]									X
Ask about any symptoms you are having or have experienced		X		X	X	X	X	X	X

[1] All attempts will be made to avoid research-only visits. Instead, sample collection will be planned to coincide with previously scheduled infusion visits, except Visit 2, which occurs at week1 and is optional.

[2] All subjects will collect a total of 4 stools at home and either mail the sample directly to the Minar Laboratory or bring the stool sample to the infusion visit

[3] You will be contacted by a member of the study staff to ask you about any symptoms you are having or have experienced, and to remind you of upcoming infusion visits.

[4] You will be given oral contrast, Breeza®, or water prior to the MRI.

Change of Mind/Study Withdrawal:

You can leave the research at any time; it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can record your reason for withdrawal.

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include significant failure to follow study procedures, if the investigator believes it is not in your best interest, or if your disease gets worse and the investigator believes it is best for you to be removed.

If you stop being in the research, data already collected may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Detailed Risks:

Risk of blood collection

When we collect blood from you for this study, you may experience slight pain at the location of the blood draw. Some bleeding, bruising or discoloration of the skin is common at the site after a blood collection. In rare instances, infection at the site may occur. The study doctor will be able to treat any symptoms your child may have.

Risk of MRI

There are no known safety risks from having an MRI for participants appropriately screened for any metal that would prohibit them from having an MRI. The study staff will review your history closely before allowing you to have the MRI. Also, some people are claustrophobic and may become anxious, fearful or nervous in the MRI scanner. No radiation is involved in an MRI. You will be given earplugs to wear during the MRI to lessen the discomfort from the noise of the MRI scanner.

Breeza® may cause diarrhea in some individuals. There could be a very rare risk of allergic reaction to ingredients.

Pregnancy Risk

The study drug has been shown to be safe throughout pregnancy. However, we are not fully aware of the effects of the study drug on unborn babies, or pregnant or breastfeeding women.

If you are pregnant, or may become pregnant, treatment with the study drug may lead to new, previously unknown, side effects, and this may involve risks to you and your unborn baby. You should tell the study doctor immediately if you become pregnant. The study doctor will follow your pregnancy to its outcome.

Privacy:

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the IRB, the Medical Monitor, your doctor, the Food and Drug Administration, and other representatives of this organization.

With your approval and as approved by the CCHMC Institutional Review Board, de-identified samples will be stored in the Minar Laboratory. These samples could be used to research the causes of Crohn's disease, its complications and other conditions for

which individuals with Crohn's disease are at increased risk, and to improve treatment. The Minar laboratory personnel will also be provided with a code-link that will link the biological specimens to each participant, maintaining the blinding.

Samples and/or data collected for or generated from this study could be shared and used for future research. Samples and /or data may be shared with other collaborators at Cincinnati Children's and possibly with outside collaborators, who may be at another institution or for-profit company.

If information that could identify you is removed from your information or samples collected during this research, that information or those samples could be stored and used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

If injured while in the study:

If you believe that you have been injured as a result of this research, you should contact Dr. Minar as soon as possible to discuss the concerns. Treatment for injuries is available at Cincinnati Children's. If you go to the Emergency Room or to another hospital or doctor, it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form.

Cincinnati Children's follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?

Cincinnati Children's Hospital Medical Center (Cincinnati Children's) will need to use and share your PHI as part of this study. This PHI will come from:

- Your Cincinnati Children's medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- Physician reports and video/photo images of a previous recorded colonoscopy

Who will share, receive and/or use your protected health information in this study?

- Staff at all the research study sites (including Cincinnati Children's)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?

You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document,

in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?

Your permission will expire at the end of the study.

Will your child's other medical care be impacted?

By signing this document, you/your child agree to participate in this research study and give permission to Cincinnati Children's to use and share you/your child's PHI for the purpose of this research study. If you refuse to sign this document, you/your child will not be able to participate in the study. However, you/your child's rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you/your child should participate in this research, you will document your permission by signature below.

You will receive a copy of this signed document for your records.

In regard to my study participation, I AGREE to the following *optional* procedures:

Initials: _____ I agree to have an MRI at Visit 8.

Initials: _____ I agree to the collection of blood at Visit 2.

_____
Printed Name of Research Participant

_____ _____
Signature of Research Participant Indicating Consent Date

_____ _____
Signature of Parent or Legally Authorized Representative* Date

_____
* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____
Signature of Individual Obtaining Consent Date