[Medical] Research Informed Consent
Title of Study: Infliximab proactive drug monitoring in the pediatric IBD population

Principal Investigator (PI): Kristen Cares, MD
Children's Hospital of Michigan
3901 Beaubien Blvd.
Detroit, MI 48201
313-745-5585

Location(s): Children's Hospital of Michigan

Funding Source: Children's Hospital of Michigan Foundation

Wayne State University/Kristen Cares, MD, is being paid to conduct this study.

When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

Key Information about this Study
You are being asked to be in a clinical research study of the use of infliximab for the treatment of inflammatory bowel disease (IBD). Your participation is voluntary (your decision). The purpose of this research study is to find out if proactive drug monitoring versus reactive drug monitoring works better for controlling IBD. If you decide to participate in this study you will be in the study for at least a year and the following procedures will be done at various time points (additional details are provided below): Measurement of your vital signs (heart rate, breathing rate, temperature, blood pressure), height and weight; we will ask you about your current health and health in the past, including any medications you are currently taking; we will ask you to complete some questionnaires about your IBD and how it impacts your life. You are already receiving infliximab for treatment of your IBD so the risks of participation are not expected to be any different than if you were not in this study. If you are assigned to the proactive monitoring group it is possible that you may experience better management of your IBD, however we cannot guarantee that participation in this study will benefit you. If you decide that you do not want to be in the study you will continue to receive infliximab and other medications for your IBD.

Purpose
You are being asked to be in a research study of inflammatory bowel disease (IBD) because you have IBD and are currently being treated with infliximab. This study is being conducted at Wayne State University and Children's Hospital of Michigan. The estimated number of study participants to be enrolled at Wayne State University and Children's Hospital of Michigan is about 60. **Please read this form and ask any questions you may have before agreeing to be in the study.**

Inflammatory bowel disease (IBD) is a chronic condition that causes inflammation of the intestinal tract. Common types of IBD include Crohn's disease and ulcerative colitis. Infliximab is a biologic medication that is approved by the U.S. Food and Drug Administration (FDA) for the treatment of IBD. Previous research with infliximab has shown it to be an effective treatment for pediatric IBD;

however, it can become less effective if the level of the medication in the body is not high enough or if a patient develops antibodies (proteins made by the immune system that attack foreign substances in the body) to the medication.

Currently, if a patient with IBD is taking infliximab and develops either abnormal lab values or reports a worsening of symptoms the doctors will measure the level of infliximab in the blood as well as any infliximab antibodies to determine if dosing changes, to either the dose of the medication or the frequency of dosing, are needed. This process is called reactive drug monitoring.

The purpose of this research study is to find out if proactive drug monitoring in patients being treated with infliximab for IBD works better for controlling IBD. Proactive drug monitoring is measuring the level of infliximab in the blood as well as infliximab antibodies before every infusion, before symptoms worsen or lab results come back abnormal, to see if dosing changes can be made that may prevent the worsening of IBD.

Study Procedures

Screening Phase:
If you decide that you would like to be in this research study, once you sign this informed consent form, the following tests and procedures will be done to make sure you qualify for the study:

- You will be asked about your current health and health in the past
- You will be asked about any medications you are currently taking, including infliximab, or have taken in the past
- We will measure your vital signs (blood pressure, heart rate, temperature, breathing rate) and your height and weight

Optimization Phase:
Once the study team determines that you qualify for the study you will begin the Optimization phase of the study. During the Optimization phase all participants will have their infliximab dose and frequency of dosing adjusted until the measurement of infliximab in the blood reaches an optimal level of 3-7µg/mL and very little or no antibodies.

If you currently receive your infliximab infusions at Children's Hospital of Michigan in Detroit, the study visits will occur the same day as your infliximab infusions and the study visits will take place in the Clinical Research Center at Children's Hospital of Michigan. If you currently receive your infliximab infusions at home or at a different location the study visits will occur the morning of or day before your scheduled infusion. You will need to travel to Children's Hospital of Michigan in Detroit for the study visits. During this phase of the study the dosing frequency of infliximab will be every 8 weeks, +/- 2 weeks, which is the same dosing frequency as in routine care. The minimum dose of infliximab that may be given is 5 mg/kg and the maximum dose of infliximab that may be given is 10 mg/kg. These doses are the same as what is currently used per routine care. The following procedures will be done at the study visits during this phase of the study:

- Measurement of vital signs (breathing rate, heart rate, blood pressure, temperature), height and weight.

_____
Parent/Guardian/Participant Initials

- Blood samples will be collected to measure infliximab levels and infliximab antibody levels as well as routine labs that are done for all patients taking infliximab.
- You will be asked to complete a questionnaire about your IBD symptoms.
- You will be asked about any medications you are taking and any medications you may have stopped or started recently.
- We will collect information about your infliximab infusion such as the dose, frequency and location.
- You will be asked about any illnesses or other health changes you have experienced

Once you reach the optimal infliximab level you will be randomly assigned to one of two groups and will enter the maintenance phase. The length of the Optimization phase will be different for each participant depending on the number of dose/dose interval changes needed in order to reach the optimal infliximab level. Some participants may begin the Maintenance phase after the first lab draw and some participants may need up to 4 dose/dose interval adjustments, which could take up to 8 months.

Maintenance phase

For the Maintenance phase you will be randomly assigned (picked by chance) to one of two groups: Standard monitoring group or infliximab level and infliximab antibody level monitoring group. All study participants will have infliximab levels and infliximab antibody levels measured prior to infliximab infusions. Your primary gastroenterologist may be blinded (he/she will not know the results of these tests) to the results of these tests depending on the group to which you are assigned.

- Group A-Standard monitoring group (Reactive drug monitoring): If you are assigned to the standard monitoring group, you will be managed the same as normally done per routine care, which involves adjusting your infliximab dose and/or dosing interval based on IBD symptoms and routine care laboratory test results. Your primary gastroenterologist will not be given the results of the infliximab and infliximab antibody level results unless your routine laboratory test results or IBD symptoms show your IBD may be worsening (If this should occur, your primary gastroenterologist will request the results of the infliximab levels and infliximab antibody results in order to adjust your dose/dosing interval accordingly).

- Group B- Infliximab level and infliximab antibody monitoring group (Proactive drug monitoring): If you are assigned to the infliximab level and infliximab antibody level monitoring group your care will be managed based on the infliximab level and infliximab antibody level results as well as your IBD symptoms and the results of routine care laboratory tests. The goal is to keep infliximab levels in the optimal range with little to no antibodies. Your primary gastroenterologist will remain blinded to the results of this test and your dose will be adjusted by one of the other study doctors who is not blinded to the results.

This phase of the study will last for about 48 weeks and the study visits will occur every 8 weeks (+/- 2 weeks). If you currently receive your infliximab infusions at Children's Hospital of Michigan in Detroit, the study visits will occur the same day as your infliximab infusions and the study visits will take place in the Clinical Research Center at Children's Hospital of Michigan. If you currently receive your infliximab infusions at home or at a different location the study visits will occur the

morning of or day before your scheduled infusion. You will need to travel to Children's Hospital of Michigan in Detroit for the study visits. The following procedures will be done at the study visits:

- Measurement of vital signs (breathing rate, heart rate, blood pressure, temperature), height and weight.
- Blood samples will be collected to measure infliximab levels and infliximab antibody levels as well as routine labs that are done for all patients taking infliximab.
- You will be asked to complete questionnaires about your IBD symptoms as well as your quality of life.
- You will be asked about any medications you are taking and any medications you may have stopped or started recently.
- You will be asked about any illnesses or other health changes you have experienced
- We will collect information about your infliximab infusion such as the dose, frequency and location.

Benefits
If you are assigned to the proactive monitoring group it is possible that you may experience better management of your IBD, however we cannot guarantee that participation in this study will benefit you. Information from this study may benefit other people with similar health issues now or in the future.

Risks
For this study you will be taking infliximab as part of the normal treatment for your IBD. The most common side effects of infliximab are infections (e.g. upper respiratory, sinusitis, and pharyngitis (sore throat)), infusion-related reactions, headache, and abdominal pain.

The following information must be released/reported to the appropriate authorities if at any time during the study there is concern that child abuse has possibly occurred.

Blood samples will be obtained from your veins. Possible side effects of obtaining blood samples are pain, bruising, bleeding, or infection at the blood draw site. Occasionally nausea, lightheadedness or fainting may occur.

There may also be risks involved from taking part in this study that are not known to researchers at this time.

Alternatives
If you decide that you do not want to take part in this study you can continue to receive infliximab and be monitored as per routine care standards.

Study Costs
You will not be charged for any tests specifically required for this research study, but you or your insurance company will be billed for the infliximab and the routine laboratory tests done for patients taking infliximab and for other tests or procedures that are considered "standard of care" and would have been part of your medical treatment if you did not participate in this study. These treatment

_____
Parent/Guardian/Participant Initials

costs include but are not limited to drugs, routine laboratory tests, x-rays, scans, surgeries, routine medical care, and physician charges.

Your health insurance company may not pay for these "standard of care" charges because you are in a research study. If your insurance company does not pay for costs associated with this research study that are considered standard care for your medical treatment, then you will be billed for these costs. You are responsible for paying for any insurance co-pays and any deductibles due under your insurance policy, and any charges your insurance company does not pay. So that you do not have unexpected expenses from being in this study, ask your study doctor for a list of the tests or procedures that will be paid by the sponsor of the study.

Compensation
You will not be paid for taking part in this study. If you currently receive your infliximab infusions at home or at a location other than Children's Hospital of Michigan the study visits will occur the morning of or day before your scheduled infusion and the visits will take place in the Clinical Research Center at Children's Hospital of Michigan in Detroit. If you have to travel to Children's Hospital of Michigan in Detroit solely for the study visits reimbursement for travel will be provided to you in the amount of $20 per study visit. It is expected that the maximum number of study visits possible is 13, therefore the total amount of compensation available if you have to travel to 13 study visits is $260.

Research Related Injuries
In the event that this research related activity results in an injury, treatment will be made available including first aid, emergency treatment, and follow-up care as needed. No reimbursement, compensation, or free medical care is offered by Wayne State University.

If a "research related injury" results from your participation in this research study, medical treatment will be provided. The costs for all your medical treatment will be billed to you and/or your insurance. A "research related-injury" means injury caused by the product or procedures required by the research which you would not have experienced if you had not participated in the research.

It is important for you to follow your physician's instructions including notifying your study physician as soon as you are able of any complication or injuries that you experienced.

You will not be paid for any other injury- or illness-related costs, such as lost wages. You are not waiving any legal rights and are not freeing the sponsor, Principal Investigator, or hospital of any malpractice, negligence, blame or guilt by participating in this study. If you think that you have suffered a research related injury, contact the PI right away at 313-745-5585.

Confidentiality
All information collected about you during the course of this study will be kept confidential to the extent permitted by law. You will be identified in the research records by a code name or number. Information that identifies you personally will not be released without your written permission. However, the study sponsor, the Institutional Review Board (IRB) at Wayne State University, or federal agencies with appropriate regulatory oversight [e.g., Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), Office of Civil Rights (OCR), etc.) may review

_____
Parent/Guardian/Participant Initials

your records. When the results of this research are published or discussed in conferences, no information will be included that would reveal your identity.

A description of this clinical trial will be available on http://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.

Voluntary Participation/Withdrawal

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you decide to take part in the study you can later change your mind and withdraw from the study. You are free to only answer questions that you want to answer. You are free to withdraw from participation in this study at any time. Your decisions will not change any present or future relationship with Wayne State University or its affiliates, or other services you are entitled to receive.

The PI may stop your participation in this study without your consent. If you have any side effects that are very serious or if you become ill during the course of the research study you may have to drop out, even if you would like to continue. The PI will make the decision and let you know if it is not possible for you to continue. The decision that is made is to protect your health and safety, or because it is part of the research plan that people who develop certain conditions or do not follow the instructions from the study doctor may not continue to participate. While taking part in this study you will be told of any important new findings that may change your willingness to continue to take part in the research.

Questions

If you have any questions about this study now or in the future, you may contact Kristen Cares, MD, or one of her research team members at the following phone number 313-745-5585. If you have questions or concerns about your rights as a research participant, the Chair of the Institutional Review Board can be contacted at (313) 577-1628. If you are unable to contact the research staff, or if you want to talk to someone other than the research staff, you may also call the Wayne State Research Subject Advocate at (313) 577-1628 to discuss problems, obtain information, or offer input.

_____

Parent/Guardian/Participant Initials

Consent to Participate in a Research Study

To voluntarily agree to take part in this study, you must sign on the line below. If you choose to take part in this study you may withdraw at any time. You are not giving up any of your legal rights by signing this form. Your signature below indicates that you have read, or had read to you, this entire consent form, including the risks and benefits, and have had all of your questions answered. You will be given a copy of this consent form.

_____ Name of Participant	_____ Date of Birth
_____ Signature of Parent/Participant/Legally Authorized Guardian	_____ Date
_____ Printed Name of Parent/ Participant/Legally Authorized Guardian	_____ Time
_____ *Signature of Parent/ Legally Authorized Guardian	_____ Date
_____ *Printed Name of Parent Authorized Guardian	_____ Time
_____ **Signature of Witness (When applicable)	_____ Date
_____ Printed Name of Witness	_____ Time
_____ Oral Assent (children age 7-12) obtained by	_____ Date
_____ Signature of Person Obtaining Consent	_____ Date
_____ Printed Name of Person Obtaining Consent	_____ Time
_____ Signature of translator	_____ Date
_____ Printed name of translator	_____ Time

* Both parent's signatures should be obtained however both are **required** for level 3 studies

** Use when parent/guardian has had consent form read to them (i.e., illiterate, legally blind, translated into foreign language).

Continue to HIPAA Authorization on next page

_____
Parent/Guardian/Participant Initials

HIPAA Authorization

A federal regulation, known as the "Health Insurance Portability and Accountability Act (HIPAA)" gives you certain rights concerning the use and disclosure (sharing with others) of your Protected Health Information (PHI). This regulation provides safeguards for the privacy and security of your information. Your permission (authorization) is required for the use and sharing of any protected health information collected as part of this research study. If you are not willing to sign this authorization to use and/or disclose your PHI by the research team, you will not be eligible to take part in this research study.

The principal investigator (PI) and her research team will use your medical records and information created or collected as part of this research study. Your PHI is important for the PI and her research team in order to collect information about you during the study, to be able to contact you if needed, and to provide treatments to you during the study, if required. The PI may send out your study related health information to the sponsor or other entities involved in this study.

Your medical records, which may contain information that directly identifies you, may be reviewed by representatives from groups identified below. The purpose of these reviews is to assure the study is being conducted properly, that data is being obtained correctly or for other uses authorized by law. These reviews occur at the study site or in the PI's research office and can take place anytime during the study or after the study has ended.

The PHI that will be "USED" for this research includes the following: name, address (street address, city, state and zip code), e-mail address, elements of dates, telephone numbers, fax numbers, social security number, medical record number, and any unique identifying numbers or characteristics or code.

The PHI that will be "DISCLOSED" or shared with others for this research includes the following: elements of dates and any unique identifying numbers or characteristics or code.

Your study information may be **used** or **shared** with the following people or groups:

- The PI, co-investigators, and key personnel of WSU associated with the research project
- WSU's Institutional Review Boards (IRB)
- Authorized members of WSU's/DMC's workforce who may need to access your information in the performance of their duties. [*For example, to provide treatment and services, ensure integrity of the research, or for accounting and/or billing matters.*]
- Other collaborating academic research institutions, which include: N/A
- The study Sponsor or representative, including companies it hires to provide study related services, which include: Children's Hospital of Michigan Foundation.
- Federal agencies with appropriate regulatory oversight (e.g., FDA, OHRP, OCR, etc.) may review your records.

Once your information has been released according to this Authorization, it could be released again and may no longer be protected by the HIPAA regulations.

_____

Parent/Guardian/Participant Initials

This Authorization does not expire. The research team may need to correct it or provide missing information about you even after the study has ended, and your medical records may be needed to assist in this process.

- During your participation in this research project you will not be able to access that part of your medical record involved in the research. This will be done to prevent the knowledge of the research results from affecting the reliability of the project. Your information will be available to the treating physician should an emergency arise that would require for him/her to know this information to best treat you. You will have access to your medical record when the study is ended or earlier, if possible. The PI is not required to release research information that is not part of your medical record.

You may withdraw (take back) your permission for the **use** and **disclosure** of your PHI for this research at anytime, by **writing** to the PI at the address on the first page of this form. Even if you withdraw your permission, the PI for the research project may still use your PHI that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission for use of your PHI, you will also be withdrawn from the research project. Withdrawing your authorization **will not** affect the health care that will be provided by the Detroit Medical Center and/or the WSU School of Medicine Practice Plans.

_____

Parent/Guardian/Participant Initials

Authorization to use and disclose PHI

- By signing this document, you are authorizing the PI to **use** and **disclose** PHI collected about you for the research purposes as described above.

Signature of participant	Date
Printed name of participant	

- For participants unable to give Authorization, the following individual is acting on behalf of the research participant (e.g., children, mentally impaired, etc.).

Signature of authorized representative	Date
Printed name of authorized representative	Relationship to the participant
Signature of person obtaining Authorization	Date
Printed name of person obtaining Authorization	Time

Nov 3, 2020

Parent/Guardian/Participant Initials