INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

Intravenous Iron for Iron-Deficiency Anemia in Pregnancy: A Randomized Controlled Trial (IVIDA)

Principal Investigator: Dr. Methodius Tuuli (317) 944-8182
IRB #: 1809251633

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. This research study will evaluate the effectiveness, safety and benefits of treating iron-deficiency anemia (low levels of iron and red blood cells) during pregnancy. Low iron and decreased red blood cells in your body can be found by testing your blood. You were selected as a possible participant because your blood was tested as part of your routine prenatal care and your results show that you have low levels of iron and red blood cells.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form and ask any questions you have before agreeing to be in the study.

This study is being conducted by Dr. Methodius Tuuli of Indiana University and in collaboration with researchers at Washington University in St. Louis.

Taking part in this study is voluntary.
You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with current or future health care providers.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to determine the safety and effectiveness of treating pregnant women with iron-deficiency anemia with either an iron infusion (medication given through an IV) or oral iron supplements (pills). Iron dextran is the intravenous (IV) medication being used in this study. Ferrous sulfate is the oral medication (pill) being used in this study. Both treatments are currently used in obstetric practice but have not been adequately compared. This study will compare these two groups to see if IV iron or oral iron is better for the mother and baby after delivery.

HOW MANY PEOPLE WILL TAKE PART?
If you agree to participate, you will be one of approximately 120 participants taking part in this study at Indiana University and Washington University in St. Louis combined. At this site, Indiana University, you will be one of approximately 80 participants. Participants will be randomly selected to either the IV iron or oral iron group with a goal of having equal numbers of participants in each group. In addition, your baby would be one of 120 newborns participating between these two research sites.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you will do the following things:

- As part of your standard prenatal care you have been screened for anemia. If you met the threshold for anemia in pregnancy, you have also been tested for iron-deficiency anemia. If you have been confirmed to have iron-deficiency anemia, you may be eligible to enroll in this study.
- If eligible, you will be assigned randomly (like flipping a coin) to one of two groups in the study:
    - Intravenous Iron Group
        - You will stop taking any oral iron supplements that were previously ordered and receive a one-time infusion of iron dextran. This infusion is made of 1000mg iron dextran that is given to you through an IV. The infusion will take place on an obstetric unit of the hospital. You will have continuous fetal monitoring throughout the infusion as well as at least 30 minutes after the infusion is completed. Fetal monitoring is a way for doctors and nurses to watch your baby's heartrate by placing a stretchy band with an electronic disk called a transducer across your abdomen. This transducer is connected to a machine and your baby's heartrate is recorded. Fetal monitoring is commonly done during labor.
        - During the iron infusion you will have a "test dose" (a small amount of medication given first) to make sure you do not have a reaction to the medication. If after 30 minutes you have no reaction, the remaining dose of medication will be given to you through the IV over the next 1-2 hours.
        - You will be called by research staff 48-72 hours after the infusion to see how you are doing and if you had any reactions or additional questions. You may skip answering any question that makes you uncomfortable.
        - There is a small chance that iron dextran will not be available due to a national drug shortage. If this happens, ferumoxytol will be substituted. When you are scheduled for your infusion, you will be notified by the scheduling unit if you will be receiving ferumoxytol instead of iron dextran. Ferumoxytol is another type of IV iron that is commonly used to treat iron-deficiency anemia. The dose given for this study will include two infusions: 510mg IV followed by another 510mg IV 3-8 days after the first infusion. These infusions will be given under the same conditions as described above. You will be contacted by research staff 48-72 hours after your second infusion to ask you about any side effects.
    - Oral Iron Supplement Group
        - You will start (or continue) taking oral iron supplements. The type of oral iron being used in this study is ferrous sulfate 325mg. You will take this pill one, two, or three times a day until delivery depending on the dose your doctor prescribes.
            - Note: If your treating doctor feels that you need oral iron supplements after delivery, you will follow your doctor's orders at that time.

        - It is recommended that these iron pills be taken either on an empty stomach or with an acidic beverage like orange juice.
        - You will be contacted by research staff two times after joining the study. The first contact will occur 2-4 weeks after you agree to be in the study; the second contact will be at delivery. Research staff may contact you in person at an existing prenatal appointment or via phone to see how you are doing and if you had any reactions to the iron. You may skip answering any question that makes you uncomfortable.
        - At delivery research staff will also ask you to report how often you were taking your iron pills while in the study.
    - Both Treatment Groups
        - Blood and data will be collected from you as part of this study. The blood collected will NOT be kept or stored for future use. Data will be collected from your baby.
            - Your blood will be drawn from a vein in your arm on admission to labor and delivery as part of your regular care whenever possible. Your blood will also be drawn again the day after you deliver your baby as part of your regular care. For this study research staff will look at the results of these blood tests in your electronic medical record.
            - We will get a blood sample from the discarded umbilical cord after delivery. This is called a cord blood sample. We will need approximately 1 teaspoon of cord blood.
            - Data will be collected from your electronic medical record and will include: demographics, medical history, diagnosis and results of anemia testing, reactions to iron infusion or supplements, delivery information, and overall health of you and your baby following delivery.
            - Data will be collected from your baby's electronic medical record and will include: gestational age at delivery, birth weight, APGAR scores (rating of your baby's health immediately after delivery), and cord blood lab results. These labs will include hemoglobin and ferritin, and may include blood gas and/or umbilical artery lactate if these tests were ordered by your treating physician. The study team will also record any unforeseen problems with your baby's health and the location of your baby after delivery (with you, NICU, etc.).
- Your participation in the study will be complete when you are discharged from the hospital and all study data has been collected.

Your pregnancy and labor and delivery management will continue to be monitored via standard of care by your regular caregiver.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, you may experience the risks, side effects, and/or discomforts detailed below.

Low Risk

1. Blood draw: Blood needed for the study will be drawn at the same time as other blood draws ordered by your doctor whenever possible to minimize your risk. Reactions to blood draw include:
    - Most common: minor pain at site, bruising
    - Less common: fainting or dizziness
    - Rare: blood clots or infection where the needle enters the skin

    *Note: There is no risk associated with collecting cord blood since the umbilical cord will be separated from you and your baby after delivery.
2. Breach of confidentiality: One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will make the best efforts to keep the information about you secure. Please see the section in this consent titled ***HOW WILL MY INFORMATION BE PROTECTED?*** for more information.

Moderate/High Risk

1. Oral iron supplement: Reactions to oral ferrous sulfate include:
    - Most common: constipation, nausea/vomiting, stomach discomfort or upset, dark stools
    - Less common: diarrhea, heartburn, urine discoloration

2. Iron infusion: This infusion will take place on an obstetric unit which is equipped with continuous fetal monitoring and emergency equipment for mother and baby if needed. This monitoring will enable your medical team to more readily notice early signs of reactions to iron dextran or ferumoxytol infusion which include:
    - Most common: discomfort and/or bruising at the site where the IV is placed
    - Less common: chest tightness, itching, urticaria (hives), flushing, nausea/vomiting, arthralgia (joint pain), back or joint aches, shortness of breath, tachycardia (fast heart rate), bradycardia (slow heart rate), cardiac arrhythmia (changes in heart rhythm), hypertension or hypotension (high or low blood pressure), shock (very low blood pressure), abdominal pain, diarrhea, peripheral edema (swelling in limbs), headache, dizziness, syncope/loss of consciousness (fainting), chills, or numbness.
        - These reactions could be delayed by 1 or 2 days after your infusion.
    - Rare: Anaphylaxis (severe allergic reaction), seizures, or non-reassuring fetal status (changes in fetal heart rate). Any of these reactions if severe could lead to maternal or fetal death.

Other Risk

You will be assigned to a treatment group by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment or other available treatments. There is a possibility that there are other risks that may not be known at this time.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

The study is not designed to provide direct benefits to you. However, study doctors have reason to believe intravenous iron may be superior to oral iron. Therefore, if you are placed into the infusion group, you may experience the benefits of reduced anemia. Additionally, results from this study have the potential to reduce anemia-related complications in pregnant women and their babies. By participating you are helping to gather these results.

WHAT ARE THE OTHER TREATMENT OPTIONS?

Treatment for iron-deficiency anemia in pregnancy is typically treated with oral iron or with IV iron, which are the two treatments being compared in this study. You do not have to be in this study to receive either of these treatments from your doctor. If you choose not to participate, your decision will not affect your clinical care.

HOW WILL MY INFORMATION BE PROTECTED?

Your privacy is very important to us. The researchers are taking many steps to protect the privacy of you and your baby. If you agree to take part in the study, a study ID number will be assigned to you and your baby. This number will be used to identify medical information kept by the study. Any records linking your name to the study ID will be stored in a locked (password protected) file.

All copies of your medical records and the links between your name and the study ID will be destroyed within fifteen years of the end of the study. After that time, your samples and information from your interviews and medical records collected for the study will be linked together with your study ID number only. Even though the information will still be used for research, it will no longer be easy to link it to you.

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study. Your identity will be held in confidence on databases in which results may be stored.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP), who may need to access your medical and/or research records.

A description of this clinical trial will be available on 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.

WILL I BE PAID FOR PARTICIPATION?

You will be given a $20 gift card at your prenatal visit when you agree to be in the study. You will receive another $20 gift card upon collection of your blood, cord blood, and data after your delivery. This gift card will be given to you at delivery if data collection is complete. If additional data is still needed at the time of your discharge, the gift card will be mailed to you.

WILL IT COST ME ANYTHING TO PARTICIPATE?

This study compares two already-accepted ways of treating iron deficiency anemia in pregnancy. Both ways are standard of care that could be prescribed during your pregnancy. Taking part in this study may lead to added costs to you or your insurance company. You or your insurance company will be responsible for the costs of either of these treatment options, including the cost of the medication and facility fees. This will be billed the same as if you were not in the study; it will be billed as part of your regular medical expenses.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher, Dr. Methodius Tuuli, at 317-944-8182. After business hours, please call the on-call OBGYN physician at 317-880-5729.

In the event of an emergency, you may call 911 or go to the Emergency Department.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

CAN I WITHDRAW FROM THE STUDY?

Taking part in this study is voluntary. If you decide to participate in this study, you can change your mind and decide to leave the study at any time in the future. The study team will help you withdraw from the study safely. If you decide to withdraw, you should contact the study team and let them know you are no longer interested in participating. You may contact the study team by phone at the number listed above or in writing to: Attn: IVIDA Study, 550 University Blvd., UH 2440, Indianapolis, IN 46202.

Your participation may be terminated by the investigator without regard to your consent if the study doctor decides it is not in the best interest of your health, if you are not following the study procedures, or if there are unforeseen circumstances that halt study activities.

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we will provide you with that information.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a signed copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____ **Date**:_____

OTHER PERMISSIONS TO CONSIDER

As part of this study we are obtaining data from you and your baby. We would like to use this data for this study as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding iron-deficiency anemia, or other diseases or conditions, including research to develop investigational tests, treatments, drugs, or devices that are not yet approved by the U.S. Food and Drug Administration (FDA). It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data you give up any property rights you may have for the data.

We would like permission to share your data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University in St. Louis, Indiana University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories at Indiana University, your name will be removed and replaced with a code. Only qualified researchers, who have received prior approval from individuals that monitor the use of the data will be able to look at your information.

If you change your mind and do not want us to store and use your data for future research you should contact the Principal Investigator identified at the beginning of this document. The data will no longer be used for future research purposes. However, if some research with your data has already been completed, the information from that research may still be used. Also, if the data has been shared with other researchers it might not be possible to withdraw the data to the extent it has been shared.

Please place your initials in the blank next to YES or NO for each of the questions below:

My data may be stored and used for future research as described above.

_____ YES **_____ NO**
Initials Initials

My data may be shared with other researchers and used by these researchers for the future research as described above.

_____ YES **_____ NO**
Initials Initials