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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Comparison of Ideal vs. Actual Weight Base Factor Dosing in Hemophilia A

PROTOCOL NO.: WIRB® Protocol #

SPONSOR: Washington State Health Care Authority

INVESTIGATOR: Rebecca Kruse-Jarres, MD, MPH
Amanda Blair, MD

SITE(S): Washington Center for Blood Disorders at Bloodworks Northwest
Seattle Children's Hospital
Oregon Health & Science University
Providence Sacred Heart Medical Center and Children's Hospital

STUDY-RELATED PHONE NUMBER(S): 206-689-6570

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

A person who takes part in a research study is called a research or study subject. As the legally authorized representative, you are being asked to provide consent on behalf of the study subject because the subject is not able to provide such consent. If the study doctor determines at a later time that the subject is able to provide consent, the subject will be asked to do so. The words "you" and "yours" in this consent form generally refer to the study subject, however, there may be some instances where "you" refers to the person providing consent.

SUMMARY

Special proteins in your blood help you to make a clot and stop bleeding when you are cut or hurt. These proteins are called clotting factors. Hemophilia happens when there is a change or mutation in a gene (small piece of your DNA) that makes a clotting factor. This change in your gene can result in low levels of clotting factor, which can result in spontaneous or prolonged bleeding. The bleeding can be treated and prevented with clotting factor concentrate. Clotting factor replacement is administered intravenously. Factor dosing is currently based on a patient's actual weight.

This study will be conducted at four locations: Washington Center for Blood Disorders at Bloodworks Northwest, Oregon Health & Science University, Seattle Children's Hospital, and Providence Sacred Heart Children's Hospital. Subjects will be recruited at these centers, and it is expected that up to twenty patients will enroll. This study is a part of the Bleeding Disorder Collaborative for Care. The Bleeding Disorder Collaborative for Care is working to improve care to patients with bleeding disorders by developing evidence-based practices related to bleeding disorders.

PURPOSE OF THE STUDY

We are conducting this study to see if the current recommended factor dosing strategy in overweight and obese patients may deliver too much clotting factor. This study will look at ways to prevent delivering too much factor by using a patient's ideal body weight as a new dosing strategy. It could be used to replace the dosing strategy of using a patient's actual body weight in overweight or obese patients. It may also help us find the safest dose for you.

PROCEDURES

In order to take part in this study, you must be a male, at least 12 years of age, and have hemophilia A. Your Body Mass Index, or BMI, must be classified as either overweight or obese for your age based on Centers for Disease Control and Prevention (CDC) definitions. You also must be willing and able to comply with the testing schedule.

In this study, you will have several blood samples taken over a period of time in order to determine how your body handles the factor product you are taking. This is called a pharmacokinetic (PK) study. The blood draws you will have for this study are referred to as PK tests. You will provide your own factor product for this study.

Prior to the first study visit after your screening visit, you will have to stop taking any FVIII (factor 8) products for either 48 hours if currently using a short-acting FVIII product, or 72 hours for a long acting FVIII product.

We will measure factor levels immediately before, and at multiple points after 2 different factor doses. At one visit, you will be given a dose of 50 U/kg for hemophilia A based on ideal body weight. At another visit, you will be given a dose of 50 U/kg for hemophilia A based on actual body weight. The order of these two doses will be determined by chance. The procedure will be the same for both tests.

The first blood draw occurs before your factor is taken, and it will measure the baseline level of FVIII in your blood. The second draw will occur 20-40 minutes after you take factor, and it will also measure the amount of FVIII in your blood. This is called the recovery level. At each draw,

you will have 1 teaspoon of blood drawn for a maximum volume of 40 ml per PK test. The table below lists the time points you will have your blood drawn.

Blood draw time points:

Hemophilia A – regular half-life product

Baseline	Measured when you arrive at clinic
Recovery - after factor is taken	20 - 40 minutes
	5 to 7 hours
	20 to 26 hours
	44 to 50 hours

Hemophilia A – extended half-life factor

Baseline	Measured when you arrive at clinic
Recovery- after factor is taken	20 - 40 minutes
	5 to 7 hours
	20 to 26 hours
	44 to 50 hours
	69 to 75 hours
	93 to 99 hours

Blood draws to measure half-life of the factor product at the remaining time points can be drawn in other local labs. If you can't come to this center, you can go to another lab. The staff here can arrange this for you. If the 20 – 40 minute recovery draw is missed at clinic, you can still be included in the study. You can have your blood drawn again within two months of the first attempt.

If you have a bleeding episode before coming to clinic, testing will be delayed until the bleed stops. If you have a bleed after any of the recovery draws, then you will need to start that PK test series again. You should treat with your regular factor regimen if a bleed occurs.

RISKS AND DISCOMFORTS

Physical Risks

When you give a blood sample, you might feel a little pain from the needle stick. You might feel light-headed or faint. Later, you might have a bruise, and there is a small risk of infection. You could be at a potentially higher risk for bleeding when taking the lower dosing at ideal body weight. If you have a bleed, treat with your usual regimen.

Privacy Risks

We do not think that there will be risks to your privacy and confidentiality by sharing your test results with the investigators.

Other Risks

NA

NEW INFORMATION

You will be told about any new information that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS

You may not receive direct benefit by being part of this study. During the study, you will gain information about factor levels in your body based on different factor dosing strategies.

COSTS

If you join the study, costs to you would include your usual insurance deductibles and co-payments. All of your insurance company's usual rules would apply. You will be asked to provide your own factor product for this study.

PAYMENT FOR PARTICIPATION

You will receive payment for your participation in this study. Please see the table below:

	Compensation
PK1: baseline visit, labs at baseline, immediately after and at 5-7 hours	$100
PK1: follow-up labs at 20-26 hrs	$50
PK1: Follow-up labs at 44-50 hrs	$50
PK1: labs at 44-50 hrs [EHL only]*	[$50]
PK1: labs at 69-75 hrs [EHL only]*	[$50]
PK2: baseline visit, labs at baseline, immediately after and at 5-7 hours	$100
PK2: follow-up labs at 20-26 hrs	$50
PK2: Follow-up labs at 44-50 hrs	$50
PK2: labs at 44-50 hrs [EHL only]*	[$50]

PK2: labs at 69-75 hrs [EHL only]*	[$50]

*****EXTENDED HALF-LIFE PRODUCT

The payments you receive for being in this study are taxable income. Your study site (either Seattle Children's or Bloodworks) is required to report to the IRS study payments of $600 or more made to anyone in any year. To make this report you will need to provide your name, address, and social security number.

ALTERNATIVE TREATMENT

The alternative is not to join the study.

CONFIDENTIALITY

If you take part, we will make every effort to keep your information confidential.

We will store all of your research records in locked cabinets and secure computer files. We will not put your name on any research data. Instead, we will label your information with a study number. The master list that links a person's name to their study number is stored in a locked cabinet or on a secure computer file.

If results of this research are published, we would not use information that identifies you.

We would only use your information for research. These are some reasons that we may need to share the information you give us with others:

- If it's required by law.
- If we think you or someone else could be harmed.
- Sponsors, government agencies or research staff sometimes look at forms like this and other study records. They do this to make sure the research is done safely and legally. Anyone who reviews study records would keep your information confidential.
    - Agencies or sponsors that may look at study records include: Study sponsor and members of research team

If you join this study, we would put information about this study in your medical record. We do this because the research study involves patient care.

We will keep your results for 7 years.

COMPENSATION FOR INJURY

If you participate in this study at Seattle Children's, and are injured as a direct result of this research study, Seattle Children's Hospital will provide treatment, or will refer you for treatment if needed. Neither you nor your insurance company will be charged for this treatment. This is

the only compensation offered for study-related injuries. It is important that you tell the study doctor, if you think that you have been injured as a result of taking part in this study. You can call the study doctor at 206-689-6570.

If you participate in this study at Bloodworks, and are injured as a direct result of this research study, Bloodworks will provide treatment, or will refer you for treatment if needed. Neither you nor your insurance company will be charged for this treatment. This is the only compensation offered for study-related injuries. It is important that you tell the study doctor, if you think that you have been injured as a result of taking part in this study. You can call the study doctor at 206-689-6570.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this research study is **voluntary**. You may decide not to participate or you may decide to leave the study at any time. Your decision will not result in any change in the medical care you will receive from your doctors and will result in no penalty or loss of benefits to which you are entitled.

You can withdraw by sending written notice to:

Rebecca Kruse-Jarres, MD/MPH
Director
Washington Center for Blood Disorders at Bloodworks Northwest
921 Terry Ave, Seattle, WA 98104

The study doctor or the sponsor may also stop your participation in the study without your consent at any time for any reason. Possible reasons may include:

- It is in your best interest.
- You do not consent to continue in the study after being told of changes in the research that may affect you.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

SOURCE OF FUNDING FOR THE STUDY

Funding for this study comes from the general fund for Washington state, appropriation funding for fiscal years 2016 and 2017 as well as the Washington State Health Care Authority's administrative account.

QUESTIONS

Contact Dr. Rebecca Kruse-Jarres at 206-689-6570 for any of the following reasons:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

If you have questions about your rights as a research subject or if you have questions, concerns, input, or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

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CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

By signing this consent form, I have not given up any of my legal rights.

[Example signature block for research involving adults able to consent, minors, and adults who lack the capacity to consent when applicable:]

Consent and Assent Instructions:

Consent: Subjects 18 years and older must sign on the subject line below
Consent is provided by the Legally Authorized Representative for adult subjects unable to consent
For subjects under 18, consent is provided by the parent or guardian

Assent: Is not required for subjects 6 years and younger
Verbal assent is required for subjects ages 7 through [14] years using the Assent section below [and the Information Sheet for Children].
Verbal assent is required for subjects ages [15] through [17] years using the Assent section below [and the Information Sheet for Adolescents].

_____
Subject Name (printed)

CONSENT SIGNATURE:

_____ _____
Signature of Subject (18 years and older) Date and Time

_____ _____
Signature of Legally Authorized Representative, Parent or Guardian (when applicable) Date and Time

_____
Authority of Subject's Legally Authorized Representative or Relationship to Subject

_____ _____
Signature of Person Conducting Informed Consent Discussion Date and Time

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ASSENT SECTION For Subjects Ages [7] - [17]:

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the subject to the best of his or her ability to understand.
2. I have answered all the questions of the subject relating to this research.
3. The subject agrees to be in the research.
4. I believe the subject's decision to enroll is voluntary.
5. The study doctor and study staff must respect the subject's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

_____ _____

Signature of Person Conducting Assent Discussion — Date and Time

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

_____ _____

Signature of Parent or Guardian — Date and Time

ASSENT SIGNATURES, For Adult Subjects with a Legally Authorized Representative:

Assent:

For adult subjects who have a legally authorized representative, I confirm that:

☐ I have explained the study to the extent compatible with the subject's understanding, and the subject has agreed to be in the study.

OR

☐ The subject is not able to assent due to lack of mental capacity.

_____ _____

Signature of Person Conducting Assent Discussion — Date and Time