Official Study Title: TRANEXAMIC ACID (TXA) TO REDUCE VOLUME OF BLOOD TRANSFUSED IN PEDIATRIC AND YOUNG ADULT CANCER PATIENTS UNDERGOING LIMB SALVAGE PROCEDURE OF A LOWER EXTREMITY

CTG Number: NCT04410042

Document Date: 06/30/2023

TRANEXAMIC ACID (TXA) TO REDUCE VOLUME OF BLOOD TRANSFUSED IN PEDIATRIC AND YOUNG ADULT CANCER PATIENTS UNDERGOING LIMB SALVAGE PROCEDURE OF A LOWER EXTREMITY (TXAKIDS)

NOTE: When we say "you" in this consent, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study or research protocol.

Key Information

To start we want to highlight the **risks and study requirements** that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

A. Why are you being asked to volunteer in this study?

You are being asked to take part in this clinical trial, a type of research study, because we would like to see if a medicine called TXA (tranexamic acid) will help slow down bleeding during surgery.

B. What is the usual approach to this condition/cancer?

Normally, surgeons may use this or another similar medicine in surgery. However, this medicine has only been tested a few times in children needing bone surgery. This medicine is approved for use in adults. Though the medicine is also approved for some usage in children, it has not been tested for or approved for use in younger patients needing limb salvage surgery.

C. Why is this study being done?

This study is being done to get information on this medicine in children. We want to see if TXA will help lower blood loss and lower the need for you to be given blood during surgery. We will look at this medicine and salt water to see which one is better for helping blood to clot.

D. What will happen if you decide to take part in this study?

You would get the TXA medicine or salt water in your intravenous vein (IV) before surgery. During surgery, the doctor will take a blood sample from you. A blood test will also be taken right after surgery and then once a day while you are in clinic. If your blood tests show that you need blood, you will be given some blood in your IV.

E. What are the research risks and benefits of taking part in this study?

The risks of surgery will be covered separately, but bleeding is common, and people usually are given blood during this type surgery. There is a chance that you will not benefit from this study. You could get low blood pressure for a while which can cause dizziness. You could have trouble with your stomach or bowels or get blurry vision.

F. How many people will take part in this study?
38 people will be in this study at St. Jude. The study will be open for 48 months.

G. What are your options?
a. Taking part in this research study is completely your choice.
b. If you decide to take part in this study, you can change your mind and stop at any time.
c. If you decide not to take part in this study, you will still receive care at St. Jude including limb sparing surgery even if you do not consent to the study.
d. You may choose no treatment or to seek treatment somewhere else.

Table of Contents

1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this clinical trial, a type of research study, because we would like to see if a medicine called TXA (tranexamic acid) will help slow down bleeding during surgery better than saltwater. This medicine has been used in many surgeries including heart, trauma, spine, hip, and knees for teenagers and adults. It has been FDA approved to use in children with hemophilia (a blood defect characterized by delayed clotting of the blood) needed for one type of surgery. However, it has not been FDA approved for this indication and potentially could have unknown or unanticipated adverse effects. Please take your time in deciding and feel free to discuss it with your family, friends and St. Jude staff. Before agreeing, it is important that you read this consent form that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital.

3. What is the purpose of this study?

The purpose of this study is to compare the amount of blood given during bone surgery when using the medicine TXA (tranexamic acid) compared to the amount of blood needed using salt water. We will also measure how much blood is lost during surgery. You may get the TXA or the salt water, the odds are even, like during a coin toss, it could go either way. Someone other than your surgeon will "flip the coin" to decide which treatment you get and only they will know. Your doctor and the helpers in surgery will not know which treatment you will be receiving.

The TXA could slow down the amount of blood that comes out of you during surgery more than the salt water does. But, it could also cause side effects, which are described in the risks section below.

This study will help the doctors and researchers find out which approach is better at slowing down how much blood is lost in surgery. The doctors will also compare how much blood needs to be given due to the surgery, both with and without the TXA medicine.

4. What will be done in this study?

After signing the consent form, you will be asked to complete some screening tests or procedures to find out if you can take part in this research study. These tests and procedures may be part of your regular care (standard of care) and may need to be done even if you cannot take part in this study. If you have had some of these tests and procedures done recently, they may or may not need to be done again. If you can take

part in the study, on the day of surgery, an IV will be placed in your arm (if you don't already have a port) and you will be given the medicine (either the TXA or the saltwater). You will receive another dose of the medicine 6 hours later. The Screening tests include:

Screening <u>Standard of Care Tests</u> (normal testing for procedure)	**Obtained Before Enrollment**	**Within 1 week of enrollment**	**Location:** surgery clinic (SC), Physical Therapy (PT)
History	**X**		**SC**
Physical exam with height & weight	**X**		**SC**
Blood tests:		**X**	**SC**
Pregnancy test	**Within 48 hours**		**SC**
Range of motion	**X**		**PT**
Functional Mobility Assessment (You use stairs and walking exercises)			**PT**
PROMIS (survey in which you explain your abilities to the researcher)	**X**		**PT**

- The total amount of blood taken during the pre-study or screening time will be about ½ tablespoon (7cc).
- If you do not qualify for this research study, you will still have your scheduled surgery and the doctor will discuss other options with you.
- Tests/ procedures that will be done during surgery, right after, and then later on are listed below.
- These tests and procedures are considered standard of care and would be done after surgery even if you're not taking part in this study:

	During Study - <u>Standard of Care (normal testing for procedure)</u>
History	**X**
Physical Exam	**X**
Blood tests	**In PACU; one-week post-op, at 6 months (end of study)**
Transfusions (the amount of blood you get is counted)	**X, if applies**
Drain output (amount)	**X**
Incisional healing (researcher describes what is seen)	**X**

Estimated Blood Loss	**X**
Blood tests	**4 hours after first dose**
Blood tests to look at chemistry	**Daily until discharge; one-week post-op; at 6 months (end of study)**
Wound follow-up	**Daily until discharge** **At 7-14 days post-op** **Every 10-14 days for "high risk" participants** **Every 7-10 days for wounds in active treatment** **At 6 weeks and 3 months for "low risk" participants** **At 6 months (end of study) for all**
Blood tests	**in PACU; Inpatient; 1 week post-op; and at 6 months post-op (end of study)**
Range Of Motion (exercise by Physical Therapist)	**6 weeks, 3 months, 6 months post-op**
Functional Mobility Assessment (using stairs and walking exercises)	**6 weeks, 3 months, 6 months post-op**
PROMIS (survey in which you explain your abilities to the researcher)	**6 weeks, 3 months, 6 months post-op**

	During Study – <u>Research (test not performed without participation in study)</u>
ROTEM (blood test that checks blood clot aspects**, for research)**	**Taken once, after surgery, for research**
Tranexamic acid (TXA)	First IV dose over 5 to 15 minutes ; second IV dose 5 to 15 to be given 6 hours later
Blood tests to look at chemistry	Post-op day 3 (only if you were discharged less than 3 days after surgery)

- The total amount of each blood draw during the study and at the end of the study will be no more than 1 tablespoon (15 cc).
- Though the study will be open for about 51 months, your part in the study will be over after your six-month post-operative study visit and exam.

5. What are the risks and benefits of taking part in this study?

a. <u>Risks</u>

<u>Study Drug:</u> Tranexamic acid (or TXA). It has not yet been firmly decided just how risky the intravenous application (IV) for the TXA drug is in children but the side effects related to receiving the medicine in your vein are listed below:

Occasional

- Skin rashes, itchiness
- Dizziness
- Low blood pressure
- Nausea
- Vomiting
- Diarrhea
- Blurry vision

Rare

- Blood clots occurring the deep vein, lungs, brain, kidneys or back of the eyes
- Eye issues such as blockage of blood to the retina of the eye and/ or visual impairment
- Seizures
- Shock
- Breathing trouble

The TXA side effects data has so far been related to adults getting the medicine by mouth, and they are listed below:

Most frequent (>10 % of the people)

- Headache
- stomach ache
- back pain
- muscular pain
- sinus or nose issues

Occasional (1-10% of the people)

- fatigue
- anemia
- muscle pain
- Cramps
- Spasms

Rare (1% of the people)

- Skin issues - itchy or scaly skin, bumps or hives on skin
- shock with low blood pressure
- seizures

- trouble breathing
- general puffiness;
- Diarrhea
- Dizzy
- Nausea
- Vomiting
- blood clot to the kidney, brain, lung, eye, kidney tube, or deep vein
- vision disturbances

Surgery: The risks involved in having your surgery are explained in a different form.

It is possible that the risk of forming a blood clot in a deep vein or developing problems with the central line function may be higher than expected in the group that receives TXA. The children in this study are at higher risk of these complications than people in previous studies using TXA because of their cancer diagnosis and the fact that they may have a central venous line.

Blood Samples:
• If an IV or central line is not present, a small needle will be inserted into the vein to obtain the blood. • Most common side effects and most likely to occur - Bleeding - Bruising or soreness • Less likely to occur but possible - Serious infection may occur

b. Benefits

You may or may not benefit from taking part in this study. However, this study treatment may help to reduce the amount of blood you lose in surgery which could make it less likely that you would need to be given blood during surgery. By taking part in this study, you may help doctors learn more about the TXA medicine for future surgeries in children and adolescents.

6. What are the risks to pregnancy, to an unborn child and to the ability to have children when taking part in this study?

Female patients who are currently pregnant or breastfeeding may not take part in this study.

7. Can you stop taking part in this study?

a. You may refuse to be in this research study or stop at any time. The decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

b. Can you be taken out of this study without your consent?

You may be taken off this study if the surgeon believes that it is best for your health or safety to no longer be in the study.

You will be taken off study at the end of all study related follow-up tests six months after surgery.

You will be taken off TXA treatment if you have a bad reaction to the first dose of the medication.

8. What are your other options?

Your other options are to have surgery without the TXA medicine. There may be other drugs that can be given to you that also help to slow down blood loss during surgery.

9. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses?

You will not be paid for your time or expenses. Also, your samples and/or information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.

11. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Michael Neel, M.D. at 901-595-3300 immediately. If you are injured from being

in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

The surgeon or researcher will tell you if any new information was learned during your study participation at the end of the study, after it is known which medicine you were given (the TXA or the salt water).

13. How will you find out the results of this study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by the 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.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

14. Will any genetic tests be done?

No genetic testing will be performed for this study.

15. What about privacy and confidentiality?

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information) may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy

Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept for a long time. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Institutional Review Board (IRB), your insurance company and other health benefits plan (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain private at all times. The information will be held securely in the password-protected study database at St. Jude. Your name will not be given to anyone else outside the research team who is not involved in the trial. You will be given a trial number, which will be used as a code to identify you on all trial forms.

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

16. Permission to Use Your Data/Information: Authorization/HIPAA

If you sign this document, you give permission to Dr. Michael Neel, his study team, the St. Jude Institutional Review Board, St. Jude Auditors and Monitors to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes all information in your medical record, results of physical examinations, medical history, lab tests, and health information relating to your surgery. The health information listed above may be used by and/or disclosed (released) to all researchers and their staff at St. Jude Children's Research Hospital.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you authorize St. Jude Children's Research Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

- You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This Authorization does not have an expiration date.

17. Further Information and Contact Details for Questions About This Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your Clinical Research Associate or surgeon, who will be able to provide you with up to date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU EXPERIENCE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT ANY OF THE DOCTORS LISTED BELOW.

Principal Investigator, Researcher, Surgeon:

Michael Neel, M.D.
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Tel: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, please let Dr. Neel or his research staff know. We care about your health. We also need to know if you've had any trouble so that we can warn others or change the way we have set this study up if that is what is needed.

You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE-IRB).

If you decide you would like to take part, then please read and sign the consent form. You will be given a copy of this information and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years): I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

_____	_____	_____AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7-13 years old)

□ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

□ Minor declined to take part in the study. The minor declined for the following reason(s):

_____

□ An assent discussion was not initiated with the minor for the following reason(s):

□ Minor is under 7 years of age.

□ Minor is incapacitated.

□ Minor refused to take part in the discussion.

□ Other_____

RESEARCH PARTICIPANT STATEMENT (14-17 years old and Adult Participants 18 years and older): I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this study.

_____	_____	_____AM/PM
Research Participant Signature	Date	Time (circle one)

RESEARCHER/DESIGNEE STATEMENT: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____	_____	_____AM/PM
Research/Designee Signature	Date	Time (circle one)
_____		
Print Name		
_____	_____	_____AM/PM
Interpreter (if needed)	Date	Time (circle one)

For non-English speaking participants, an interpreter is required. The interpreter may serve as the impartial witness.

Research Participant's Advocate Statement

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented/agreed to take part in the research.

_____ _____ _____*AM/PM*

Research Participant Advocate *Date* *Time* *(circle one)*

PLEASE SEND THE COMPLETED CONSENT FORM TO CLINICAL TRIALS OPERATIONS

SCAN AND E-MAIL THE CONSENT TO protocoleligibilityoffice@stjude.org

Or FAX to (901) 595-6265