

Consent Version date: 9/7/2016

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**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO -- FRESNO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY**

Study Title: Intraoperative Administration of Tranexamic Acid for Placenta Previa and Accreta Study (TAPPAS): A Randomized, Placebo-controlled Trial

This is a medical research study led by Dr. Kremer from the UCSF Fresno Department of OBGYN. Dr. Kremer and/or her research team will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you (a) have a suspected accreta based on imaging studies (ultrasound or MRI study), or (b) are at high risk for having a placenta accreta (for example, at least two prior c-sections with a low lying placenta previa). Placenta accreta is a condition in which the placenta abnormally invades or grows into the uterine wall. Placenta previa is a condition in which the placenta is lying unusually low in the uterus, next to or covering the cervix.

Why is this study being done?

Surgeries done for patients with placenta previa or accreta are high risk and involve a higher amount of blood loss than normal c-sections. Often, placenta accreta requires complete removal of the uterus (hysterectomy) after performing a c-section to control bleeding. Today, there are no medications commonly used to reduce blood loss in patients with these high risk surgeries.

The purpose of this study is to determine if intravenous tranexamic acid (TA) is effective for reducing blood loss during surgical procedures in women at high risk for hemorrhage due to placenta previa or placenta accreta. TA is not currently FDA approved to treat blood loss during C-sections; however, it is commonly used in other types of surgery for patients who are expected to have a large blood loss, such as hip replacements or open heart surgery.

The current standard of care for patients at high risk for having a placenta accreta or patients suspected of having a placenta acreta is to perform the surgery at a tertiary care hospital with experienced surgeons and operating room teams, with access to blood products if transfusion is needed. Sometimes, a surgeon will also request placement of balloons in the arteries leading to the uterus to attempt to lower blood loss. You will be receiving the standard of care regardless of whether you choose to participate in the study.

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How many people will take part in this study?

Placenta previa with multiple prior c-sections, and placenta accreta is very rare. About 60 people will take part in this study.

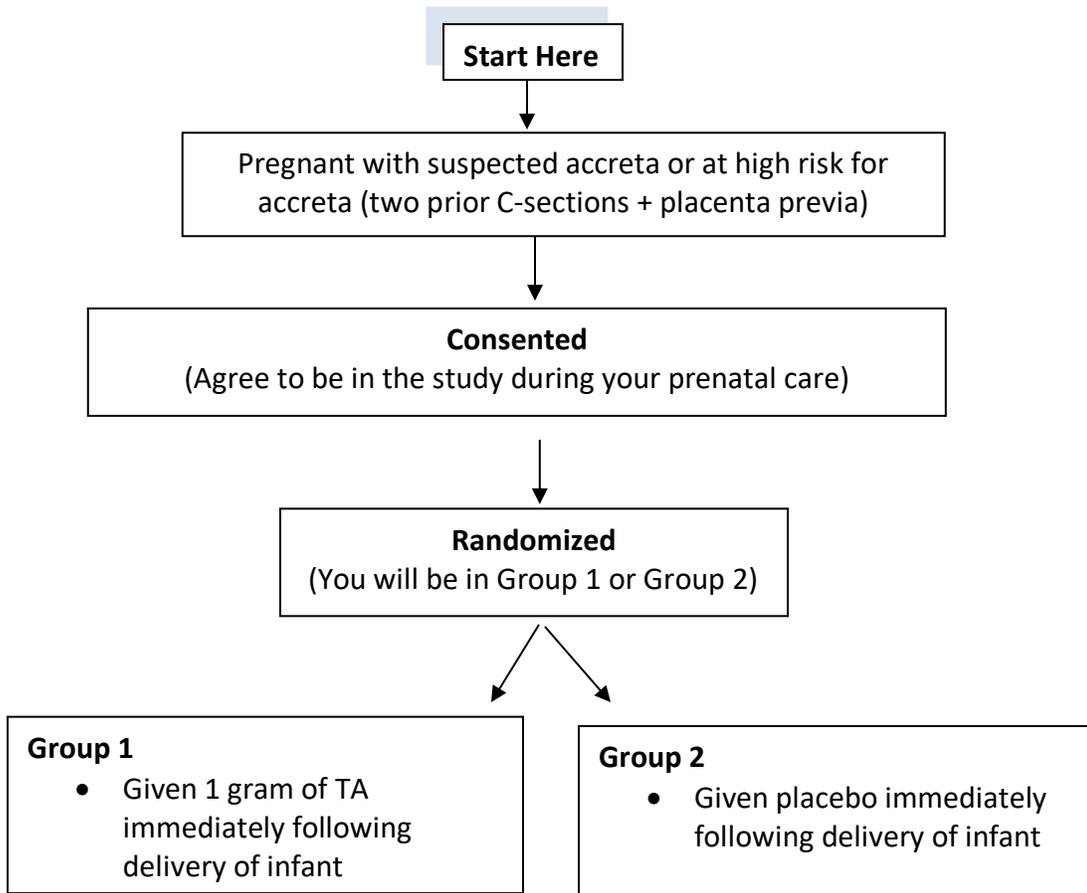
What will happen if I take part in this research study?

All study procedures will be done at Community Regional Medical Center. You will be randomized into one of the study groups described below. Randomization means you are put into a group by chance. The investigators will randomize you electronically into one of the groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in any group.

- **If you are in group 1:** You will be given 1 gram of intravenous TA in your IV immediately after delivery of the infant.
- **If you are in group 2:** You will be given a placebo (no study drug) in your IV immediately after delivery of the infant.

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



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After your surgery, study investigators monitor you throughout your hospital stay and follow up with you at your routine post-operative visits.

How will information about me be kept confidential?

Information will be collected from your medical records. Only study-approved investigators, the Community Medical Centers' Institutional Review Board, or federal and state regulatory groups will be able to look at or copy medical records. Study records that identify you will be kept confidential and you will be assigned a unique code number.

Some information from your medical records will be collected and used for this study. If you do not have a medical record, one will be created for you. Your signed consent form will be added to your medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation.

How long will I be in the study?

Participation in the study begins after consent and concludes with your last post-operative visit. The study drug, however, will only be administered once during your surgery. All other study related follow ups will be during your routine hospital visits.

What are my responsibilities?

As a research participant you will be asked to follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in the study changes.

Can I stop being in the study?

Yes. You have the right to stop being in the study, without loss of benefits to which you are otherwise entitled. This means that you can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. She will tell you how to stop your participation safely.

What side effects or risks can I expect from being in the study?

Below are the risks of participating in this study:

1. Stress or worry from participating in a study. Please remember at any time you can choose to stop participation.
2. Risk of Randomization: You will be assigned between two different treatment groups by chance, and the treatment you receive may prove to be less effective or have more side effects than the other study group.

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3. Risk of placebo: If you are in the group that receives placebo, your surgical procedure will proceed without the additional study drug treatment.
4. Unknown risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Everyone taking part in the study will be watched carefully for any side effects. Tranexamic Acid (TA) medicine may cause some unwanted side effects. Although not all of these side effects may occur, if they do occur they may need medical attention. Many side effects go away shortly after the drugs are stopped, but in some cases side effects may be serious, long lasting, life threatening or result in death. You should talk to your study doctor about any side effects you experience while taking part in the study. For more information about your condition and research-related injury or about this study you may contact Dr. Kremer at 559-499-6549.

Tranexamic acid (TA) is safe and has been studied before in pregnant and postpartum women to reduce bleeding after vaginal deliveries and in women with cesarean sections. All pregnant and recently pregnant (also known as post partum) women have an increased risk of blood clots in the legs or lungs. In prior studies in these women, TA did not increase the risk of blood clots in the legs or lungs (deep vein thrombosis or pulmonary embolism) beyond your baseline risk. However, the drug is not thought to be safe to use in patients who have **active** (pre-existing) blood clots in the legs or lungs (deep vein thrombosis or pulmonary embolism) or in women with blood clotting disorders or in women with active bleeding in the brain. These women will not be able to participate in the study. The drug also can have a rare side effect of changes in color vision. For this reason, women who are already color-blind cannot participate in the study.

Tranexamic acid can be passed into breast milk in very small concentrations but it is safe to participate in the study if you plan to breastfeed or pump. About 1% of the drug levels in your blood can be detected in breast milk one hour later. The drug has a short "half life", which means that it is present in your body for a short period of time, and is present at significant levels in your blood for only about 2-11 hours after the last dose is given.

Check with your doctor immediately if any of the following side effects occur:

Infrequent: (percentages for how often these side effects occur are not available by the drug manufacturer)

- Diarrhea, nausea, or vomiting
- Low blood pressure
- Inflammation of skin caused by an allergic reaction
- Blurred vision
- Giddiness

Rare (occurring less than 1% of the time):

- Severe allergic reaction (anaphylaxis)
- Problems with eyesight (color vision changes)
- Blood Clots in the legs or lungs

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- Seizure
- Dizziness or lightheadedness, decreased alertness
- Problems with the kidney or the ureter (due to blood clot formation)

For more information about the risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

If tranexamic acid is effective in reducing blood loss, the benefit would be less blood loss, less need for blood transfusion, and possibly fewer other complications related to blood loss in surgery (bleeding disorders, low temperature). Also, even if the drug is not effective or helpful to you, the benefit for all participants is to increase our knowledge about ways to treat heavy operative bleeding from placenta previa or placenta accreta for women in the future.

If you are in the group that receives TA and it proves to treat your condition more effectively than the placebo, you may benefit from participating in the study, but this cannot be guaranteed.

What other choices do I have if I do not take part in this study?

If you wish not to take part in the study, you will receive the standard care for your condition without being in the study and will not lose any benefits to which you are otherwise entitled.

To end your participation in this study, you must contact the study doctor at the contact information listed on page 1 of this informed consent form. Your participation in this study is voluntary. If you do join the study, you may leave the study at any time. Your decision to participate will not change your relationship with your doctor or the hospital.

The study doctor in charge of the research study can remove you from this study without your consent for any reason, including, but not limited to:

- a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
- b. Your failure to follow the instructions of the study staff.
- c. If the study is stopped by the sponsor, study doctor, IRB, or FDA.

Will my medical information be kept private?

We will take every precaution to make sure that the personal information in your medical record is kept private and secure. However, we cannot guarantee complete privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- UCSF's Committee on Human Research

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- Community Medical Centers' Institutional Review Board (a committee charged with the protection of human subjects in research)
- The University of California
- Food and Drug Administration
- Office for Human Research Protections
- Department of Health and Human Services
- Community Medical Centers

What are the costs of taking part in this study?

The will be no additional cost to you for participation. You will not be responsible for the cost of the study drug. You will have to pay for any costs not covered by your health insurer.

Will I be paid for taking part in this study?

You will receive a \$20 gift card for your participation after you consent and are enrolled in the study.

Are there any financial conflicts on the part of the researchers?

The study was awarded a grant to cover costs of conducting the study. The researchers are not getting financial compensation for this study. There is no financial conflict of interest.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Kremer if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at (559) 499-6549.

Treatment and compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University of California does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415-476-1814. You may also contact the Community Medical Centers IRB office at (559) 499-6653 for further information.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

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In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about this study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. For information about your disease, about research – related injury, or about this study, you may contact Dr. Kremer at (559) 499-6549. For information about your rights as a research subject, you may contact the Chair of Community Medical Centers (CMC) Institutional Review Board (IRB) at (559) 499-6653.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at (415) 476-1814 or the CMC IRB at (559) 499-6653.

For additional information about this clinical trial you can visit www.clinicaltrials.gov. ClinicalTrials.gov is a website that provides information about clinical trials. 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.

CONSENT

You have been given a copy of this consent form and the Experimental Subject’s Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Printed Name of Subject

CMC Medical Record #

Subject’s Signature for Consent

Date Signed/Time

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Printed Name of Witness

Witness Signature

Date Signed/Time

Investigator's Signature Below

Printed Name of Person Obtaining Consent

Date Signed/Time

Signature of Person Obtaining Consent

Investigator Printed Name

Date Signed/Time

Investigator Signature

CMC's Interpreter Statement:

In the event that an interpreter is needed: I have accurately and completely read the

foregoing document to: _____ in _____
(Patient or Legal Representative Name) (Language Used)

She understands all terminology/conditions, acknowledges her agreement by signing the document in my presence.

Printed Name/Signature of Interpreter

Date Signed/Time

Participant Initials: _____

CALIFORNIA EXPERIMENTAL SUBJECT’S BILL OF RIGHTS

California law requires that any person asked to take part as a subject in research involving a medical experiment, or any person asked to consent to such participation on behalf of another, is entitled to receive the following list of rights written in a language in which the person is fluent. This list includes the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedure to be followed in the medical experiment and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of the signed and dated written consent form.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject’s decision.

For questions about patient rights, contact the Chairman of the Institutional Review Board at Community Medical Centers at (559) 499-6552.

I have carefully read the information contained above and I understand fully my rights as a potential subject in a medical experiment involving people as subjects.

Printed Name/ Signature (Subject)

Date/Time

Printed Name/ Signature (Witness)

Date/Time

Participant Initials: _____

USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

Protected Health Information is any personal health information through which you can be identified. A decision to participate in this research means that you agree to the use of your health information for the purposes explained in this consent form. By signing this form, you are authorizing the use and disclosure of your health information collected in connection with your participation in this research study. Your information will only be used in accordance with the provisions of this consent form and applicable law.

Your health information related to this study, including your entire medical record, may be used or disclosed in connection with this research study. Study records that identify you will be kept confidential as required by law. Except when required by law, you will not be identified by name, SS#, address, phone#, or any other direct personal identifier in study records disclosed outside of the Community Medical Centers (CMC). For records disclosed outside of CMC, you will be assigned a unique code number. The key to the code will be kept in a locked file in the office of the Principal Investigator, Dr. Kremer.

Representatives of the following groups are authorized to use and/or disclose your health information in connection with this research study:

- The principal investigator, Dr. Kremer, her research team, and all Sub-Investigators
- The Community Medical Centers Institutional Review Board
- The University of California
- Community Medical Center

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office of Human Research Protections
- Department Of Health and Human Services
- Federal and State Regulatory Groups
- Food and Drug Administration

EXPIRATION DATE OR EVENT FOR THE RETENTION OF RECORDS

The study results will be retained in your research record for at least six years or until after the study is completed, whichever is longer. At that time either the

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research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at Community Medical Centers. Any research information in your medical record will be kept indefinitely.

VOLUNTARY PARTICIPATION

Your participation is voluntary and you may choose not to participate in this research study or withdraw your consent or authorization for the use and disclosure of your health information at any time. Your choice will not at any time affect the commitment of your health care providers to administer care and there will be no penalty or loss of benefits to which you are otherwise entitled. If you decide to end your participation in the study, please notify the researcher(s) in writing.

If you have questions or concerns regarding your privacy and the use of your personal health information, please contact the Privacy Officer, at 559-459-2742.

Printed Name/ Signature (Subject) Date/Time

Printed Name/ Signature (Witness) Date/Time

Participant Initials: _____