"Can Ondansetron Prevent Neonatal Abstinence Syndrome (NAS) in Babies Born to Narcotic-dependent Women (AIM2NAS)"

Maternal Informed Consent

NCT# 01965704

Date of IRB approval of the ICF: April 26, 2016

IRB Use Only
Approval Date: April 26, 2016
Expiration Date: April 26, 2017

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Are you participating in any other research studies? _____ Yes _____No

PURPOSE OF RESEARCH

You are invited to participate in a research study of the Prevention of Neonatal Abstinence Syndrome (NAS) because we believe your baby may be at risk to develop NAS and you just signed the parental permission to allow your baby to participate in this study. NAS is a combination of symptoms that develop in a baby who is born to a mother who is dependent on (using) narcotics every day (examples of narcotics: methadone, morphine, codeine, oxycodone, vicodin).

We hope to learn if we can prevent or lessen Neonatal Abstinence Syndrome in the babies born to mothers dependent on narcotics, by giving the mothers a dose of intravenous (IV) ondansetron prior to delivery, followed by giving their babies up to 5 days of oral (PO) ondansetron. Ondansetron is an FDA approved drug for use in pregnant women and in children to prevent nausea. In this study, the study medication given to you is not for prevention of nausea; but to prevent NAS in your newborn baby. Half of the mothers in this study will receive ondansetron, and half will receive placebo (an inactive liquid that contains no medicine and looks identical to the ondansetron).

This is a "double-blind study", meaning neither you or your doctor will know which one of the two study medications you will receive; only the pharmacist who prepares the study drug will know what you receive.

You were selected as a possible participant in this study because you are a pregnant woman, currently using a daily narcotic medication, in generally good health and with no known history of problems with the rhythm of your heart, 18 through 45 years old, having one baby, and planning to deliver at Stanford's Lucile Packard Children's Hospital when the gestational age of the fetus is between 37 to 42 weeks.

If you decide to terminate your participation in this study, you should notify Dr. Drover at 650-725-0364.

This research study is looking for 90 pregnant women who are dependent on narcotic drugs and the 90 babies born to these mothers. The study will be done at multiple sites (approximately 5-10 sites) across the United States of America with Stanford as the coordinating center. LPCH/Stanford Hospital expects to enroll 30 of the 90 research study participants.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

DURATION OF STUDY INVOLVEMENT

Your participation will start on the day you deliver your baby. As soon as your baby is born, his or her participation will begin as well while they are being treated with the study medication with the purpose of preventing Neonatal Abstinence Syndrome (NAS).

The total time for you and your baby to be involved in the study may be up to 35 days: up to 5 days of study drug administration for your baby in the hospital; 10 daily phone calls or visits, depending on whether your baby is at home or in the hospital, for follow-up; and a final follow-up phone call or visit about 30-35 days after your baby's last dose of study medication.

The entire study is expected to take 2-3 years to complete.

PROCEDURES

If you choose to participate, the Protocol Director and his research study staff will explain the study in detail to you and obtain your written consent to participate on this form. You have already signed the parental permission form to allow your baby to participate once the baby is born. The following procedures will occur for you, after written consent is obtained:

Mother's Participation on Delivery Day:

1. A urine sample will be obtained, before you deliver your baby, for a drug screen to determine all drugs in your system. If the drug screen is positive for an illicit drug and was subpoenaed or somehow disclosed, an unlikely event, it could be incriminating.

2. Study Medication: you will receive a dose of study medication, either ondansetron 8mg or placebo (an inactive liquid that contains no medicine and looks identical to the ondansetron) through an intravenous line (IV) within 4 hours of delivering your baby. If you have not delivered your baby within 4 hours of receiving the study drug, a second dose will be given.

a. Which of the two study medications you receive will be determined by a randomization schedule. This is like flipping a coin, you will have a 50% chance of receiving ondansetron and a 50% chance of receiving placebo (45 mothers will receive ondansetron and 45 mothers will receive placebo).

3. One blood sample (approximately 1 teaspoon) will be drawn within 30 minutes of your delivery (either before or after delivery) to measure levels of ondansetron and the metabolites (what ondansetron breaks down to once it is in your body). Any blood samples left over after analysis will be destroyed when the study is completed.

4. Follow up phone calls. Once you have delivered your baby we will ask questions about the feeding and activity of your baby. For example: How many times and for how long each time do you feed your baby? Are you breastfeeding, formula feeding, or a combination of both? Is the baby crying excessively? Is the baby gaining weight? Is the baby having diarrhea?

5. With your permission, we would like the name of your baby's pediatrician and/or other healthcare provider (such as, public health nurse) in case we need to contact them about your baby's health. We would contact your baby's healthcare provider only if we were concerned that your baby might develop neonatal abstinence syndrome after leaving the hospital, and would let you know that we contacted them.

6. If you have a history of having problems with your heart's rhythm we may order a 12-lead electrocardiogram (ECG) to make sure your heart rate and rhythm are within normal ranges prior to delivery. We will pay for this ECG.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Take the study drug as directed.
- Be available for our daily phone calls after you are sent home.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you or the baby may have after you go home.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

There is no risk to you or the baby if you change your mind and decide to stop the study early.

If you decide to withdraw your consent to participate in this study, or the study medication is stopped for any reason, there are no anticipated problems, but you should notify Dr. David Drover at 650-725-0364 as soon as possible.

The Protocol Director may also withdraw you from the study and the study medication may be stopped, without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you or your baby.
- You or your baby needs treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

Because you would likely receive ondansetron or some other anti-nausea medication in the course of your standard clinical care for the delivery of your baby (whether by Cesarean Section or by vaginal delivery), the risks associated with the medications and ondansetron are not changed because of the study. Single doses of ondansetron range from 4 mg to 16 mg, depending on the reason for administration, making the study dose of 8 mg well within the safe therapeutic range for nausea. However, we are not giving you the study medication to prevent or treat your nausea, we are giving you the study medication to get the study medication into your unborn baby. We want to get the study drug in your baby prior to delivery so your baby will be born with the study drug in their system. If you should need a medication specifically for nausea prior to delivery, you will receive another anti-nausea medication, not ondansetron, because ondansetron is one of the study medications.

The side effects of ondansetron are:

Common Reactions
* headache
* constipation
* fatigue
* diarrhea
* hypoxia (decrease in oxygen in your system)
* pyrexia (increased body temperature)
* urinary retention
* dizziness
* agitation
* pruritus (itching)

Serious Reactions
* severe hypersensitivity reaction
* anaphylaxis (extreme allergic reaction that can be life threatening)
* bronchospasm (spasm of the muscles around your "wind pipe")
* extrapyramidal symptoms (changes effecting the nerves controlling your motor activity)
* oculogyric crisis (uncontrolled rolling of your eyes)
* blindness, transient
* QTc prolongation (change in the way your heart beats)

The possible risks of obtaining a blood sample from you are pain and bruising. Infection can also occur anytime the skin is broken to obtain samples, but this risk is extremely small as sterile supplies are used, and all hospital protocols are followed.

The 12-lead ECG for you poses no risk other than a very slight risk of possible skin irritation where the sticky pads are placed on your skin.

This particular treatment may involve risks to the subject, which are currently unforeseeable.

POTENTIAL BENEFITS

There is no direct benefit to you by participating in this study. Our belief is that the knowledge we gain from this study will benefit medical research about NAS and how to prevent it in the future. Your baby's participation will be spelled out in a separate Parental Permission Consent Form. This consent form is only for your participation in the study.

We cannot and do not guarantee or promise that you will receive any benefits from this study.

ALTERNATIVES

- The alternative is not to participate.
- We will not withhold any standard treatments for you or the baby.
- Please discuss the potential risks and benefits of not participating with a physician.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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.

CONFIDENTIALITY

Your identity will be kept as confidential as possible as required by law. Your personal health information related to this study may be disclosed as authorized by you. Your responses to questions concerning illegal drug use could be self-incriminating and harmful to you if they became known outside the study. As explained in this confidentiality statement of the consent, we do not intend to disclose this information. Your research records may be disclosed outside of Stanford, but in this case, you will be identified only by a unique code number. Information about the code will be kept in a secure location and access limited to research study personnel.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity will not be disclosed**.**
We will do everything we can to keep others from learning about your participation in this study. To further help us protect your privacy, we received a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS) on Aug 21, 2013, which was prior to enrolling any participants.

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you or your child, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, your child, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of this study is to determine if the drug ondansetron, if given to babies born to narcotic-dependent mothers, will prevent those babies from suffering from a syndrome called "Neonatal Abstinence Syndrome", also called "NAS". We hope to learn if we can prevent NAS by first giving these pregnant narcotic-dependent women a dose of intravenous (IV) ondansetron prior to the delivery of their babies, followed by giving the newborn babies a dose of ondansetron once a day for up to 5 days. Currently there is no standard-of-care medicine used to "prevent NAS" and babies are only treated once they suffer the symptoms of withdrawal from narcotics. Because this is a clinical trial, the information will be submitted to the sponsor, the National Institutes of Health (NIH), and the Food and Drug Administration (FDA).

Do I have to sign this authorization form?
You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study, including receiving any research-related treatment. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?
If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: David R. Drover, MD. Stanford Medical Center, Anesthesia Department, MC 5117, 300 Pasteur Drive, Stanford, CA 94305.

What Personal Information Will Be Obtained, Used or Disclosed?
Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to, for the pregnant narcotic-dependent women: one blood sample for analysis of ondansetron, one possible ECG, one urine drug screen prior to delivery; name, medical record number, demographic information (such as, date of birth, height, weight, ethnicity, race, pregnancy history), medication history (including any prescription meds, any street drugs and any narcotics used in the 2 months prior to delivery and through 1 month following delivery), medical and surgical history, tobacco history, and name and contact information of baby's pediatrician and/or other healthcare provider (such as public health nurse); frequency and duration of breast/bottle feeding in hospital and at home after discharge, and all other drugs taken for 1 month after delivery while breast/bottle feeding the baby.

Who May Use or Disclose the Information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, David Drover, MD
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

Who May Receive or Use the Information?
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 for Human Research Protections in the U.S. Department of Health and Human Services
- National Institutes of Health (NIH)
- The Food and Drug Administration (FDA)
- Data Safety Monitoring Board

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?
Your authorization for the use and/or disclosure of your health information will end on (December 31, 2025) or when the research project ends, whichever is earlier.

Will access to my medical record be limited during the study?
To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (e.g., if included in your official medical record).

_____ _____
Signature of Adult Female Participant Date

Print Name of Adult Participant: _____

FINANCIAL CONSIDERATIONS

Payment
You will not be paid to participate in this research study.

Costs
If you participate in this study, there may be additional costs to you. These include the personal time it will take to come to all of the study visits.

The study will pay for those services, supplies, procedures, and care associated with this study that are not a part of your routine medical care. If you would like to review the list of such covered services, supplies, procedures and care, please tell us now or at any time during the study.

Participation in this study is not a substitute for health insurance. You and/or your health insurance must pay for those services, supplies, procedures, and care that you require during this study for routine medical care. **You will be responsible for any co-payments and/or deductibles as required by your insurance.**

Sponsor
The National Institutes of Health (NIH) is providing financial support and/or material for this study.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Contact information should include the following as appropriate.
Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. David Drover at (650) 725-0364. You should also contact him at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, 3000 El Camino Real, Five Palo Alto Square, 4th Floor, MC 5579, Palo Alto, CA 94306.

Alternate Contact: If you cannot reach the Protocol Director, please contact Dr. Brendan Carvalho at 650-861-8607 or pager number 650-723-8222, ID #13980.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- 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.

May we contact you about future studies that may be of interest to you?

____ Yes ____ No

Signing your name means you agree to be in this study and that you were given a copy of this consent form.

_____ _____
Signature of Adult Female Participant Date

Printed Name of Adult Participant: _____

_____ _____
Signature of Person Obtaining Consent Date

Printed Name of Person Obtaining Consent: _____

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.

_____ _____
Signature of witness Date

Print Name of Witness: _____

(e.g., staff, translator/interpreter, family member, or other person who speaks both English and the participant's language)

- Translated short form must be signed and dated by both the participant (or their LAR) AND the witness.
- The English consent form (referred to as the "Summary Form" in the regulations):
  - Must be signed by the witness AND the Person Obtaining Consent (POC).
  - The non-English speaking participant/LAR does not sign the English consent.
  - The non-English speaking participant/LAR should not sign the HIPAA participant line
  - If the participant or the LAR is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the LAR's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.