Ulipristal acetate for use in early pregnancy loss: A Phase 2 pilot feasibility study

Informed Consent Document
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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: 2/15/2022
IRB Study # 21-2315
Title of Study: Ulipristal acetate for use in early pregnancy loss: A Phase 2 pilot feasibility study
Principal Investigator: Jill Hagey
Principal Investigator Department: Obstetrics and Gynecology-Family Planning
Principal Investigator Phone number: 919-962-4880
Principal Investigator Email Address: jill.hagey@unchealth.unc.edu
Faculty Advisor: Amy Bryant
Faculty Advisor Contact Information: 9849741592

CONCISE SUMMARY

The purpose of this research study is to determine if ulipristal acetate (UPA, also known as "Ella®") can be used in treatment of pregnancy loss in the first trimester. You are being approached to participate in this study because you have undergone a pregnancy loss and have decided to take medication to help the pregnancy pass from the uterus.
If you choose to participate, you will take a pill called ulipristal acetate, which is an FDA-approved medication for emergency contraception, during your visit with the research team. Then, you will take another medication, misoprostol, by placing tablets in your vagina 6 to 18 hours after you take the ulipristal acetate. Approximately one to four hours after taking the misoprostol, you can expect to start having bleeding and cramping heavier than a period as you pass the pregnancy.
You will have a follow up visit two to three days after you take the misoprostol in our clinic to complete an ultrasound to make sure the pregnancy has passed. If the pregnancy has not passed, you'll be offered options on what you'd like to do to help the pregnancy pass including watching and waiting, taking another dose of the misoprostol medicine, or having a surgical procedure. If you have not yet passed the pregnancy, you will have another follow up visit the next week to complete an ultrasound to make sure the pregnancy has passed. All study participants will have a follow-up phone call in one month to ask about your experience.
Risks of the study include headache, nausea and abdominal pain; as well as bleeding and cramping when the pregnancy is passing.
If you are interested in learning more about this study, please continue reading below.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness,

you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to understand if ulipristal acetate (UPA, also known as "Ella®") can be used with misoprostol to help women experiencing pregnancy loss to pass their pregnancy. The combination of UPA and misoprostol used in this study is investigational which means it is not approved by the Food and Drug Administration (FDA) to treat pregnancy loss in the first trimester. Right now, women who take medication to pass their pregnancy can take either misoprostol alone or misoprostol with another medication, mifepristone, that is similar to ulipristal acetate.

You are being asked to be in the study because you have experienced a pregnancy loss in your first trimester of pregnancy. You have decided that you would like to take medication to help pass your pregnancy.

Are there any reasons you should not be in this study?

You should not be in this study if you have already started to pass your pregnancy or if your doctor thinks that you are not safe to pass your pregnancy at home. Other reasons you should not be in the study include if you have a pelvic infection, low blood counts (severe anemia), a known heart disease, a known bleeding or clotting disease, or if you take blood thinner medication.

How many people will take part in this study?

Approximately 40 people at UNC-Chapel Hill will take part in this study.

How long will your part in this study last?

You will be involved in this study for one month. You will take the study medication, ulipristal acetate, today with the research staff. You will then take another medication, misoprostol, at home 6 to 18 hours after you take the ulipristal acetate. Women generally start having bleeding and cramping to pass the pregnancy one to four hours after taking the misoprostol. You will have one or two follow up visits in the next week at the UNC Family Planning Clinic to complete an ultrasound to confirm that the pregnancy passed. These visits will take approximately 30 minutes. You will have a laboratory test in two weeks to assess your liver function. This visit will take approximately 10 minutes. You will have a phone call approximately one month after taking the medications with our research staff to discuss your experience with the medication. This phone call will take approximately 15 minutes.

What will happen if you take part in the study?

Enrollment Visit:

- You will complete a paper questionnaire with questions about your health history and your pregnancy history. You may choose not to answer a question for any reason.

- You will have your liver function assessed prior to administration of the study medication.
- You will be given three pills of ulipristal acetate to take by mouth by the study team.
- You will be given a prescription for four pills of misoprostol to take at home. You will put all four pills of misoprostol in your vagina 6 to 18 hours after taking the ulipristal acetate. Most women experience bleeding and cramping one to four hours after taking the misoprostol as you pass the pregnancy. The heaviest bleeding generally lasts one day. You can take pain medications (ibuprofen and Tylenol) and medications for nausea to treat your symptoms while you are passing the pregnancy.

Follow Up Visit:

- You will have a follow up visit at the UNC Family Planning Clinic approximately 2 to 3 days after you take the misoprostol medication.
- You will have a transvaginal ultrasound to look at your uterus and confirm that you passed the pregnancy.
- If you did not pass all the pregnancy, you will be offered to watch and wait for the pregnancy to pass on its own, take another dose of the misoprostol medicine, or have a surgical procedure. If you do not pass all the pregnancy, you will come back to the UNC Family Planning Clinic for a second follow up visit approximately 5 days after your first visit.

Follow Up Laboratory Visit:

- You will have a follow up laboratory visit at a UNC lab convenient to you approximately 2 weeks after you take the study medications.

Follow Up Phone Call:

- You will be called by one of our research staff approximately 1 month after you participate in the study. The research staff will ask you questions about any additional treatments you took to help pass the pregnancy, any side effects you experienced with the medication and what you thought of the experience.

Participation in the study is voluntary and you will receive treatment for your pregnancy loss regardless of your participation in the study. Drs. Jill Hagey and Amy Bryant are responsible for patient welfare during the study.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study. We will ensure that you get appropriate treatment for your pregnancy loss.

What are the possible risks or discomforts involved from being in this study?

Ulipristal acetate is FDA approved for emergency contraception and has been studied for safety. Possible risks associated with taking ulipristal acetate include headache, nausea, abdominal pain, fatigue, dizziness and acne. Possible risks associated with taking misoprostol include diarrhea, abdominal pain, vaginal bleeding and cramping. Possible risks associated with transvaginal ultrasound include discomfort with the procedure.

Heavy bleeding following administration of misoprostol may be a sign of incomplete passage of your pregnancy or other complications and prompt medical or surgical intervention may be needed. Please seek immediate medical care and contact the study doctor listed on the first page of this form should this occur.

There are some concerns regarding the hepatic safety of ulipristal acetate and few cases of liver injury have been reported with long term use of ulipristal acetate. We will assess your liver function tests prior to administration of ulipristal acetate and at two weeks after the study medication. We will also monitor you for signs and symptoms of liver toxicity (fatigue, abdominal pain, nausea and vomiting, jaundice). Risks of having blood drawn to monitor your liver function tests include pain, bruising, and fainting.

There is a risk of breach of confidentiality, although all efforts will be taken to protect your information. All study materials will be kept solely with the study staff.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

What are the risks to a pregnancy or to a nursing child?

We do not know the effect of the study drug on babies before they are born, or on nursing children. Many drugs can get into the mother's milk. You should not breastfeed your child while taking the study drug. You may return to your normal fertility quickly after you pass your pregnancy. There is no known risk to a future pregnancy from taking the study drug.

If you choose not to be in the study, what other treatment options do you have?

You do not have to be in this research study in order to receive treatment. The other procedures or treatments that are available for your pregnancy loss include watching and waiting to see if the pregnancy passes, taking similar medications to help the pregnancy pass (mifepristone and misoprostol), or having a surgical procedure to remove the pregnancy from the uterus.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Whenever imaging (e.g. MRI, CT, X-ray, ultrasound, etc.) is done, there is the chance of finding something unexpected. Unexpected findings can have clinical significance, or no clinical significance. Clinically significant means that the imaging shows a problem that may require further follow up or treatment. The imaging in this study will be reviewed by a qualified radiologist. You will be informed of any findings of clinical significance that may be discovered during the imaging procedure.

There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate). The imaging we are using in this research study is not the same quality as the imaging that you may have as

part of your health care. If you believe you are having symptoms that may require clinical imaging, you should contact your primary care physician.

Will I receive any other clinical results?
Other clinically relevant results of this research will be communicated with you at the time of your follow up visit regarding the outcome of your transvaginal ultrasound and whether you passed your pregnancy to discuss next steps in care.

How will information about you be protected?
All research materials will be documented on paper questionnaires that will be stored in a secure, locked cabinet only accessible to study staff. Information from these paper questionnaires will be transcribed onto a secure data server that is housed at UNC. Only research staff will have access to this data. Information about your care for early pregnancy loss will be documented in your UNC electronic medical record (EPIC). As part of this study, you will be asked if the research staff may access your electronic medical record to document the care you receive for your pregnancy loss and to follow up if you have any complications or side effects during the course of your treatment.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

For participants for whom Spanish is their first language, we will use a hospital-approved bilingual interpreter during our study activities to maintain confidentiality.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside

funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do. By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?

You will receive reimbursement for your time and transportation for the one or two follow up visits that you complete at the UNC Family Planning Clinic. You will be reimbursed US $20 for each visit that you attend, up to two visits. You will also receive a parking voucher for your follow up visits. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?

If you enroll in this study, you will have costs which include:

- Enrollment Visit
    - Ulipristal acetate and misoprostol will be paid for by the study sponsor and provided to you by the research team.
    - Your OBGYN physician will provide you with pain medication and nausea medication to help keep you comfortable while you pass your pregnancy at home. These medications may be covered by your insurance, or you may have to pay a small fee for them.
- Follow Up Visit
    - Your visit will be performed for research purposes only and will be covered by the study sponsor. The study sponsor will pay for the clinic visit and the transvaginal ultrasound.
    - If you do not pass the pregnancy and require either an additional dose of misoprostol medication or a surgical procedure to remove the pregnancy, these costs will be billed to you or your insurance carrier.
    - You will be given US $20 to reimburse for your travel costs and time for the visit. You will receive a parking voucher to attend your follow up visit at the UNC Family Planning Clinic.
- Follow Up Laboratory Visit
    - Your visit will be performed for research purposes only and will be covered by the study sponsor.
    - The study sponsor will pay for the laboratory visit and blood testing.
- Follow Up Phone Call
    - There are no costs associated with this phone call.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

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.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you

would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness if applicable; e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness