Official title:

Treatment of unfavorable bleeding patterns in contraceptive implant users: a randomized clinical trial of curcumin

Principal Investigator:
Alison Edelman, MD, MPH

NCT No:
04205929

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Approval Expires: 9/15/2023

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

IRB#: 20645

CLINICAL RESEARCH CONSENT SUMMARY

TITLE: Treatment of unfavorable bleeding patterns in contraceptive implant users: a randomized clinical trial of Curcumin

PRINCIPAL INVESTIGATOR: Alison Edelman, MD MPH (503) 494-2585

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of the study is to learn more about a dietary supplement that may be helpful in reducing vaginal bleeding that women can have when using the contraceptive implant (Nexplanon or Implanon).

DURATION:
Your participation in the study will consist of 3 visits over 60 days. Visits will last up to 2 hours.

PROCEDURES:
If you decide to take part in this study, you will get either the study "drug", Theracurmin HP-Max, or placebo for up to 30 days. You will be asked to have a number of tests and procedures such as physical exams, pregnancy tests, gonorrhea and chlamydia tests, respond to a daily text message or email diary, and have your vitals assessed.

RISKS: At the highest doses this supplement can cause nausea and diarrhea but we are using a lower dose in this study. The supplement may also not be effective in helping to treat your bleeding.

BENEFITS: You will not benefit from being in this study. However, by serving as a research participant, you may help us learn how to benefit patients in the future.

ALTERNATIVES: There may be alternative therapies you could try with your doctor to help with your bleeding. You may choose not to participate in this study.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

IRB Approved: 9/21/2022
Approval Expires: 9/15/2023

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MED. REC. NO. _____
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Clinical Research Consent and Authorization Form

TITLE: Treatment of unfavorable bleeding patterns in contraceptive implant users: a randomized clinical trial of Curcumin

PRINCIPAL INVESTIGATOR:	Alison Edelman, MD MPH	(503) 494-2585
CO-INVESTIGATORS:	Jeffrey Jensen, MD MPH	(503) 494-5113
	Marci Messerle Forbes, FNP	(503) 494-6151
	Andrea O'Donnell, FNP	(503) 494-3131

WHO IS PAYING FOR THE STUDY?: Merck Women's Health Investigator Initiated Studies Program

WHO IS PROVIDING SUPPORT FOR THE STUDY?:
Your study doctor and the research staff have no financial involvement with the funder and are not being paid directly by the funder for conducting this study. However, they may have travel expenses covered by the funder to attend study training meetings.

WHY IS THIS STUDY BEING DONE?:
You have been invited to be in this research study because you are between 15 and 45 years old, currently using the contraceptive implant (Nexplanon, Implanon) for birth control, and are experiencing a lot of bleeding and/or spotting in the last 30 days. The purpose of the study is to learn whether Curcumin, an active part of the spice Turmeric, may reduce vaginal bleeding or spotting. The investigational drug is called Theracurmin HP-Max (300 mg Theracurmin, 50 mg ginger root, 4mg Bioperine). You will take two doses of the study drug at a time (600 mg Theracurmin, 10 mg ginger root, 8mg Bioperine). Theracurmin HP-Max will be called "the study drug" throughout this form.

There are currently no medications approved to treat vaginal bleeding in women using the contraceptive implant. The study drug may reduce bleeding.

The use of the study medication for vaginal bleeding/spotting is experimental. It has not been approved by the FDA because we do not know enough about it and the FDA does not regulate dietary supplements.

This study requires 3 visits to the research clinic at OHSU and may take up to 60 days to complete. We plan to enroll up to 80 women.

We are asking you to provide information for a data bank, also called a repository. The information collected will include your demographic information, medical history, and bleeding diary. This information will be stored indefinitely and may be used and disclosed in the future for research. You may choose to participate in the study but not the repository.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?

Screening Visit:

At the first study visit you will answer questions about your medical and pregnancy history. Vitals will be performed: height, weight, blood pressure, and pulse. A urine pregnancy test will be performed. You will answer questions about your vaginal bleeding over the last 3 months. You will have a brief physical exam including a pelvic exam. The purpose of the pelvic exam is to make sure you don't have another reason to have too much vaginal bleeding, such as an infection. We will perform a test for gonorrhea or chlamydia (sexually transmitted infections or STIs) which can also cause women to have unanticipated, mid-cycle vaginal bleeding. If you have not had a pap smear within the recommended time, we will complete this test. You will not be charged for these tests. They will be part of your OHSU medical record. This visit will take about 1.5-2 hours.

Enrollment Visit:

The second study visit will take place as soon as your pap and/or gonorrhea & chlamydia test results are available. Our study coordinator will call or email you to schedule this visit. Blood pressure and a urine pregnancy test will be performed. Study drug will be provided to you at this visit. You should start taking the study drug on the third day of your next bleeding episode. That means that when you next have bleeding or spotting every day for three days, start the study drug. At this visit if you are currently bleeding, the coordinator will have you fill out this information on a paper diary and if you have had 3 days in a row of bleeding or spotting, then study drug can be started immediately at this visit. If you have only had 1 or 2 days, this will be noted and the study coordinator will explain the earliest day that you could start the study drug. Once you start it, you should take it every day, even if your bleeding stops. If your bleeding or spotting does not last three days or more, you should not start taking the study drug.

At your enrollment visit, you will learn how to track and report your bleeding via text messaging and how to take the study drug or placebo.

Bleeding diary (via text or email):

Every day you are in the study, you will be asked to keep a record of your vaginal bleeding. You will receive a text message on your cell phone or an email every day at the same time (8pm). The message will ask about your bleeding for the day. You should respond to this message using the number code provided. This should take only a few seconds each day. If you do not respond to the electronic diary, you will receive a phone call or email from the study coordinator to check in.

You will be given a paper diary (calendar) as an "emergency" back-up to the text message. Please fill out this paper calendar if you are unable to access the texting or email service for any reason (travelling, out of cell range, etc). You will be asked to communicate with the study team immediately if you have to switch to the paper diary method at any point during the study.

Study drug:

While you are in the study, you will take two doses of the study drug or placebo for 30 days. You have a 50% chance of receiving the study medication or placebo. A placebo is a pill that looks like the study drug but has no real medicine in it. This part of the study is a randomized study. Neither you nor the study staff can choose whether you get the study drug or the placebo. You and the study staff will not know which pill you are taking. The study is done this way because knowing whether you are getting the study drug can change the results of the study. If you start having serious side effects from the study drug, or if you became pregnant while participating in this study, the investigators can find out what you are taking in order to help you. Please ask the study staff if you have any questions at all about this kind of study.

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If your period or vaginal bleeding lasts 3 days:

- Start taking the study drug on the third day in a row of bleeding or spotting
- Take two of the study drug daily for 30 days, even if your bleeding or spotting stops.
- You will receive a text message or email every day asking if you took the study drug that day. You should respond to this message using the number code provided. A study coordinator will contact you if you are reporting 3 days of bleeding or spotting but do not report taking the study drug.

If your period or bleeding does NOT last 3 days or longer:

- Do not start taking the study drug.

Visit 3 (End of study visit): The final visit will take place approximately 30 days after you started taking study drug or up to 60 days after enrollment or at the time of study withdrawal/exit.

If you do not have any bleeding within 30 days of the enrollment visit, you will not take study drug and will exit the study.

Repeat STI testing will be done only if indicated by a change in partners during the study. Vital signs will be performed and a review of bleeding diary, medications, and health changes. A short satisfaction questionnaire will be performed. Participation is complete after this visit. Unused study drug will be returned at this visits.

Visit	**Details**
Visit 1 – Screening	• Informed consent • Review medications • Confirm implant use • Physical exam with vitals (blood pressure, pulse, weight, height) • Urine pregnancy test • Review eligibility criteria • Gonorrhea and chlamydia test • Pap (if indicated) • Baseline questionnaire
Visit 2 – Enrollment	• Review bleeding diary with staff • Review medications • Vitals (blood pressure, pulse, weight, height) • Confirm implant use • Receive placebo or study drug and instructions • Review any health changes
Visit 3 – End of study	• Urine pregnancy test if indicated • Repeat Gonorrhea and chlamydia test if change in partner occurs during study. • Review medications • Return any unused medication • Vitals (blood pressure, pulse, weight, height) • Confirm implant use • Review bleeding diary with staff • Review health changes • Exit questionnaire

It is possible that your medical record will be reviewed if you participate in this research study. The information that would be collected includes your use of contraception (such as placement or removal of the implant), and laboratory records such as pap smears or STI testing.

If you have any questions regarding this study now or in the future, contact Alison Edelman, MD at (503) 418-2585 or other members of the study team at (503) 494-3666.

WILL I RECEIVE RESULTS FROM THE TESTING IN THIS STUDY?
You will receive the results of your pap test and STI test, and pregnancy test results done through out the study. We do not plan to share your research test results with you or your primary care provider. However, if we discover information that is important for your health care, either in this study or in the future, we will contact you and ask if you want to know the results. If you choose to receive the results, you may need to have the test repeated in a non-research laboratory. You may learn information about your health that is upsetting or that impacts your family planning decisions.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:
You will not benefit from being in this study. However, by serving as a research participant, you may help us learn how to benefit patients in the future.

The study drug is extremely well tolerated even up to extremely high doses and is considered safe by the FDA. At the highest doses, which we are not utilizing here, a few subjects reported nausea and diarrhea.

If you are nursing an infant or you are pregnant now, you must not be in the study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. If you become pregnant during the research study, please tell the investigator and your doctor immediately.

There are several drugs (prescription and non-prescription) that may cause problems when taken with the study drug. The study staff will carefully review all of the drugs you are taking before giving you the study drug. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the study staff before you take the new drug. You could also have that provider talk to the study staff before prescribing the new drug. Do not take any new over-the-counter drugs while you are in this study unless you first check with the study staff.

Some parts of the study may be inconvenient. We are asking you to respond to two messages every day. These are regular text or email messages and will count towards text messages or data in your cell phone plan. You will be asked detailed questions about your bleeding and your gynecologic history. Some of these questions may seem very personal or embarrassing. You may refuse to answer any of the questions that you do not wish to answer.

Text messages are not fully secure and, while every effort is made to limit content that could identify you, text messaging increases the risk that your health information could be compromised. By agreeing to receive these texts, you are assuming liability of that increase. If you do not want to receive text messaging you may receive your study diary via email.

Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?
You may choose not to be in this study. There may be alternative therapies you could try with your doctor to help your bleeding.

WHO WILL SEE MY PERSONAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. A code number will be assigned to you and your information. Only the investigators and people involved in the conduct of the study will be authorized to link the code number to you.

We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, Merck & Co., and the funder's representatives
- The Food and Drug Administration
- The Office for Human Research Protections, a federal agency that oversees research involving humans
- The company that helps us send messages about bleeding (Mir3). This company will only receive your phone number or email address and no other personal information.

Those listed above may also be permitted to review and copy your records, including your medical records.

We may also share your information with other researchers, who may use it for future research studies.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

OHSU complies with Oregon state requirements for reporting certain diseases and conditions to local health departments.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Data from this study may be shared with other investigators for future research studies. This is optional, see Optional Section below. A code number will be assigned to you as well as to information about you. Only the investigators and people involved in the conduct of the study will be authorized to link the code number to you. Other investigators who may receive samples of your medical information for research will be given only the code number which will not identify you. We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT?

Information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost to you or your insurance company to participate in this study with one exception. The exception is that you will be responsible for any costs incurred on your cell phone bill as a result of receiving study text or email messages.

You will be compensated up to $250 for your participation in this study. Compensation breakdown is as follows:

- Visit 1 - Screening: $50
- Visit 2 - Enrollment: $50
- Visit 3 - Study end $50
- Diary Completion: $100

You may receive payment via a debit card. There may be fees (for example, if the card is inactive for more than six months), which will be deducted from the balance on your card. Details on how to use the card and any fees are included in the separate card member agreement and FAQ sheet.

We may request your social security number in order to process any payments for participation.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:

If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact the study coordinator or principal investigator at 503-494-2811, or OHSU at 503-494-9000.

If you are injured or harmed by the study drug or study procedures, you will be treated. OHSU and Merck & Co**.** do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

WHERE CAN I GET MORE INFORMATION?

If you have any questions, concerns, or complaints regarding this study now or in the future, contact Dr. Alison Edelman at 503-418-2585 or call 503-494-8311 and ask the operator to have the operator page her. Or, you may contact other members of the study team at 503-494-3666.

This research has been approved and is overseen by an Institutional Review Board (“IRB”), a committee that protects the rights and welfare of research participants. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

WHAT ARE MY RESPONSIBILITIES IN THIS STUDY?

We will ask you to complete a daily diary of when you take study medication and if you have any bleeding or spotting.

DO I HAVE TO TAKE PART IN THIS STUDY?

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research participant in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Alison Edelman, MD
Oregon Health & Science University
3181 SW Sam Jackson Park Road, Mailcode UHN-50
Portland, OR 97239
edelmana@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If you choose to withdraw from the study, you will be asked to return any remaining study drug. You will be asked to answer a short series of questions about your bleeding and satisfaction.

If you choose to have your contraceptive implant removed while participating in the study, you will need to return to your gynecologic provider for removal. The study will not pay for implant removal. We will ask you to return for a final study visit before your implant is removed. At this time we will ask you to return any remaining study drug. We will ask you questions about your bleeding and satisfaction.

If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from *your samples and information, b*ut the material will not be destroyed and we will continue to use it for research.

You may be removed from the study if the investigator or sponsor stops the study, you become pregnant, you develop serious side effects, or you do not follow study instructions. You will be removed from the study if you do not have 3 consecutive days of bleeding or spotting and do not initiate study drug within the first 30 days of enrollment.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

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.

SIGNATURES:

PARTICIPANT OPTION

_____ I give my consent for my data to be stored in a repository and used and disclosed for future research studies.

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Subject Printed Name (or Parent/Gaurdian if subject is uner 18)	Subject Signature (or Parent/Gaurdian if subject is uner 18)	Date

Relationship to subject

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Subjects ages 15-17:

Your signature below indicates that you agree to be in this study.

Subject Printed Name	Subject Signature	Date