Informed Consent

Study Title: Epidiolex (CBD) in Patients With Biochemically Recurrent Prostate Cancer

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	7/28/2020
NCT Number:	NCT04428203
IRB Number	56982
Coversheet created:	10/4/2021

KEY INFORMATION FOR MCC-19-GU-74-PMC: A phase I/Ib Study on the Safety of Epidiolex in Patients with Prostate Cancer with Rising PSA after Localized Therapy with either Surgery or Radiation

We are asking you to choose whether or not to volunteer for a research study about the long-term safety and tolerability of Epidiolex in patients with biochemically recurrent prostate cancer. Biochemical recurrence is a condition where PSA levels rise after treatment for prostate cancer.

You are being asked to take part in this study because you have previously completed localized therapy (prostatectomy or radiotherapy) for prostate adenocarcinoma and your PSA level has risen. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn about the short-term side effects as well as the long-term safety and tolerability of different Epidiolex (CBD) doses in patients with biochemically recurrent prostate cancer. We also want to see whether taking Epidiolex (CBD) results in changes to your PSA and testosterone levels. Epidiolex is a CBD oil product FDA approved for the treatment of seizures associated with two rare and severe forms of epilepsy. Epidiolex is not approved for the treatment of prostate cancer but previous studies have shown that it may lower PSA levels. Your participation in this research will last about 120 days.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Taking part in this study may or may not make your health better. The information from this study will help doctors learn more about using Epidiolex for treatment in prostate cancer and could lead to better treatments in the future. Previous studies suggest that Epidiolex may lower your PSA and/or testosterone levels. For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may not want to take part in this study if you are unwilling to stop using non-study related CBD oil, Marinol or marijuana use while on-study. If you are currently using these products, you will have to stop them for a week before going on study. If you are currently depressed or if you have a history of depression, you should discuss this with the study doctor as Epidiolex may worsen these symptoms. You should not take part in this study if you have a history of hypersensitivity to CBD products. You may not want to participate in this study because of the side effects listed in the detailed consent below. For a complete description of risks, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Zin Myint, M.D of the University of Kentucky, Department of Internal Medicine at 859-323-3964 or by mail at University of Kentucky Markey Cancer Center, 800 Rose Street, Lexington, KY 40536

If you have any concerns or questions about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?
You would not qualify to participate in this study if you are:

• Under the age of 18
•You are currently taking any other investigational agents
•You are unwilling/unable to discontinue use of CBD oil products, Marinol or marijuana
• There are other criteria that must be met to take part in this study that your study doctor will review with you.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at University of Kentucky Medical Center and Markey Cancer Center facilities. You will need to come six times during the study. Each of those visits will take about 3 hours. If your disease worsens while you are on the study, you will stop study treatment. If this happens, you will be asked to come in for a final off-study visit that will take about an hour. The total amount of time you will be asked to volunteer for this study is 18 hours over the next 120 days.

WHAT WILL YOU BE ASKED TO DO?

You will be asked if you are interested in taking part in this research study. If you are interested, you will be asked to read this informed consent form and ask any questions you may have and decide whether you want to take part in the study. If you agree to be in the study, you will be asked to sign and date the last page of this form. You will be asked to come in six times for this study. First, you will be asked to come in once for pre-study screening visit to determine if you can join the study, four times for Epidiolex administration, and finally once for follow up after treatment is complete. If your disease progresses (worsens), you will be asked to come in for a final "off-study" visit. See below for detailed list of what will occur at each visit:

Pre-Study Visit (Screening)

- The study doctor will ask you about your medical history, including any medicines, herbal/natural remedies, vitamins, or other over-the-counter (e.g., aspirin) items that you have taken in the last 90 days or are taking now. Demographic information will also be collected.
- You will have a full physical examination performed by a medical doctor to check your health status. Your blood pressure, heart rate, the number of times you breathe per minute, your body temperature (known as vital signs), and your height and weight will be measured. The study doctor will assess the state of your cancer and how the disease affects your daily living. The doctor will also ask you about any thoughts you may have about death or harming yourself.
- You will be asked to complete two questionnaires about your health.
- You will be asked to provide a sample of your blood (about 3 tablespoons, or 45 milliliters) for routine tests to evaluate your overall health, organ function as well as your PSA and total testosterone levels.
- You will be asked to provide a urine sample. It will be screened for the presence of THC, which is the compound in cannabis that is psychoactive.
- Electrocardiogram (abbreviated as EKG or ECG) is a test that measures the electrical activity of your heartbeat.
- If you have previous had a biopsy, your archival tumor will be tested to learn more about the Cannabidiol (CBD) levels present in that tissue.
- The scans (PET, CT, MRI, etc.) that you received as part of your standard care will also be used to determine whether you are eligible to be in this study.

All lab tests and scans should be completed within 4 weeks of starting treatment.

Treatment

Day 1 of taking Epidiolex

If you are eligible to take part in this study, you will be asked to come in for the following procedures.

- You will take Epidiolex by mouth, once a day, on empty stomach on an outpatient basis using the dose assigned to you by the study doctor. You will be asked to maintain a medication diary of each dose of medication. The medication diary will be returned to clinic staff at the end of each course.
- Once you have started the study, the status of your cancer will be assessed using standard scans. If your PSA rises or you experience other clinical systems, the study doctor may ask you to have scans to determine if your cancer is progressing (worsening).
- You will be asked to provide a sample of your blood (about 3 tablespoons, or 45 milliliters) for routine tests to evaluate your overall health and organ function.
- If necessary, you will have a full physical examination to check your health status, assess the state of your cancer and to determine how your disease affects your daily living.

Day 30, Day 60 and Day 90 after you begin taking Epidiolex

You will be asked to come in for a visit 30, 60 and 90 days after you begin taking Epidiolex.

- You will take Epidiolex by mouth, once a day, on empty stomach on an outpatient basis using the dose assigned to you by the study doctor. You will be asked to maintain a medication diary of each dose of medication. The medication diary will be returned to clinic staff at the end of each course.
- The study doctor will ask you about any side effects you have experienced since the previous visit.
- The study doctor will ask you about your medical history, including any medicines, herbal/natural remedies, vitamins, or other over-the-counter (e.g., aspirin) items that you have taken in the last 90 days or are taking now.
- You will have a full physical examination to check your health status. Your blood pressure, heart rate, the number of times you breathe per minute, your body temperature (known as vital signs), and your height and weight will be measured. The study doctor will assess the state of your cancer and how the disease affects your daily living. The doctor will also ask you about any thoughts you may have about death or harming yourself.
- You will be asked to provide a sample of your blood (about 3 tablespoons, or 45 milliliters) for routine tests to evaluate your overall health, organ function as well as your PSA and total testosterone levels.
- Electrocardiogram (abbreviated as EKG or ECG) is a test that measures the electrical activity of the heartbeat.
- During the study, the status of your cancer will be assessed using standard scans. If your PSA rises or you experience other clinical systems, the study doctor may ask you to have scans to determine if your cancer is progressing (worsening).
- You will be asked to complete two questionnaires about your health (Day 90 visit only).

30 days after your last dose of Epidiolex

- The study doctor will ask you about any side effects you have experienced.
- You will be asked to provide a sample of your blood (about 3 tablespoons, or 45 milliliters) to evaluate your PSA and total testosterone levels. If your doctor thinks it is necessary, she may perform routine tests on your sample to evaluate your overall health and organ function.
- During the study, the status of your cancer will be assessed using standard scans. If your PSA rises or you experience other clinical systems, the study doctor may ask you to have scans to determine if your cancer is progressing (worsening).
- If you doctor feels it necessary, you will have a full physical examination to check your health status. Your blood pressure, heart rate, the number of times you breathe per minute, your body temperature (known as vital signs), and your height and weight will be measured. The study doctor will assess the state of your cancer and how the disease affects your daily living. The doctor will also ask you about any thoughts you may have about death or harming yourself.

If you begin Androgen deprivation therapy (ADT) at any time during this study, you will be taken off study treatment.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

These side effects are very common but not everyone will necessarily experience them

- Decreased appetite
- Diarrhea
- Transaminase elevations (changes in your bloodwork that can signify liver damage)
- Fatigue
- Malaise (feeling uncomfortable, ill or lack of energy but you cannot explain the cause)
- Asthenia (physical weakness or lack of energy)
- Rash
- Infection
- Insomnia
- Somnolence (sleepiness or drowsiness)
- Mood changes including depressive symptomatology and sometimes suicidal ideation

Allergic Reactions

As with any drug, it is possible that you could have allergic reactions to study drug, such as itching, skin rash, facial swelling, and/or a severe or sudden drop in blood pressure. A sudden drop in blood pressure could lead to loss of consciousness and/or possible seizures and could progress to the possibility of significant side effects including death. If you have any of the above symptoms, seek medical attention right away.

Blood Sampling

Having blood drawn from a vein in your body may cause some pain, soreness, possible fainting, bleeding, redness, or bruising where the needle is inserted. An infection is also possible, but rare. If you feel faint while having your blood drawn, you should sit or lie down to avoid falling.

Electrocardiogram (ECG)

Your skin may react to the sticky patches that attach the detectors (electrodes) to the chest for the ECG. This skin irritation usually disappears when the patches are removed

Reproductive Risks

You should not father a baby while on this study because Epidiolex may involve risks to the embryo or fetus. If your partner becomes pregnant anytime during the study or within 3 months after stopping the study drug, you must immediately tell your study doctor.

Other Risks

There is always a chance that any medical intervention can harm you. In addition to the risks listed above, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

There is no guarantee that you will get any benefit from taking part in this study. Your willingness to take part, however, may, in the future, help doctors better understand and/or treat others who have your condition.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to take part in the study, there are other choices such as:

- Getting treatment or care for your cancer without being in a study. Standard of care at the University of Kentucky for your cancer may include observation or intermittent hormonal therapy;
- Taking part in another study of an investigational drug;
- Getting no treatment.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare, or Medicaid will be responsible for the costs of all care and treatment that you would normally receive for any conditions you may have. These are costs that are considered medically necessary and will be part of the care you receive even if you do not take part in this study.

The University of Kentucky may not be allowed to bill your insurance company, Medicare, or Medicaid for the medical procedures done strictly for research.

Therefore, these costs will be paid for by Markey Cancer Center, the sponsor of this study:

- The costs associated with providing the study drug (Epidiolex)
- Biomarker correlative tests analysis

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

When we write about or share the results from the study, we will write about the combined information. We will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. At the University of Kentucky, data is stored at the Markey Cancer Center in locked facilities, and with limited access to records by designated research staff. The study doctor will assign you a unique code consisting of a series of numbers and only your unique code, and nothing that could identify you personally, will be entered into the study report forms.

You should know that in some cases we may have to show your information to other people because of state or federal law.

For example, the law may require us to share your information with:

- a court or agencies, if you have a reportable disease/condition;
- authorities, if you report information about a child being abused; or if you pose a danger to yourself or someone else.

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

- The University of Kentucky Institutional Review Board
- Representatives of the U.S. Food and Drug Administration as required by law
- Representatives of the National Cancer Institute (NCI)
- Representatives of the Kentucky Cancer Registry
- Authorized representatives of the University of Kentucky, UK Hospital, and the Markey Cancer Center

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study.

If you withdraw or are withdrawn, the study drug will no longer be provided free of charge and may not be available commercially.

If you choose to leave the study early, data collected until that point will remain in the study database and may not be removed.

The investigators conducting the study may need to remove you from the study. You may be removed from the study if:

- you are not able to follow the directions,
- we find that your participation in the study is more risk than benefit to you, or
- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may not take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Zin Myint, M.D. at 859-323-3964 immediately. If you should have an emergency after 5pm during the week or on the weekend, please contact UK Paging Operator at (859) 323-5321 and ask to page Dr. Zin Myint and she will determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Medical costs related to your care and treatment because of study-related harm will be your responsibility;

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will not receive any rewards or payment for taking part in the study.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Generally, tests done for research purposes are not meant to provide clinical information. We will not provide you with individual research results.

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 18 people to do so at the University of Kentucky.

The Markey Cancer Center is providing financial support and/or material for this study.

A description of this clinical trial will be available on 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.

WILL YOUR INFORMATION (OR SPECIMEN SAMPLES) BE USED FOR FUTURE RESEARCH?

Your information or samples collected for this study will NOT be used or shared for future research studies, even if we remove the identifiable information like your name, medical record number, or date of birth.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Gender
- Race
- Age
- Results of physical exams, blood tests, X-rays, tumor measurements, tissue analysis and other diagnostic and medical procedures;
- Your medical history, medical information about your disease and medical information pertaining to your condition; and other diagnostic and medical procedures related to the study.
- Information on side affects you may experience and how these were treated;
- Long-term information about your general health status and the status of your disease;
- Medicare Health Insurance Claim Numbers (HICN), Social Security Numbers (SSN) and Employer Identification Numbers (EIN) if regulated by Medicare reporting provisions.

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies when required by law;
- University of Kentucky representatives;
- UK Hospital
- Food and Drug Administration (FDA)
- Investigational Drug Service (IDS
- Center for Clinical and Translational Science (CCTS)
- National Cancer Institute (NCI)
- Kentucky Cancer Registry
- Markey Cancer Center
- Your primary physician will be contacted if the researcher, in the course of the project, learns of a medical condition that needs immediate attention.

The researchers agree to only share your health information with the people listed in this document.

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:

- Current or future healthcare at the University of Kentucky;
- Current or future payments to the University of Kentucky;
- Ability to enroll in any health plans (if applicable); or
- Eligibility for benefits (if applicable).

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- Send a written letter to: Zin Myint, M.D. University of Kentucky Markey Cancer Center, 800 Rose Street, Lexington, KY 40536 to inform her of your decision.

- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

You will not be allowed to review the information collected for this research study until after the study is completed. When the study is over, you may have the right to access the information.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Monday-Friday at (859) 323-1184.

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____ **Signature of research subject**	_____ **Date**
_____ **Printed name of research subject**	
_____ Printed name of [authorized] person obtaining informed consent and HIPAA authorization	_____ Date
_____ Signature of Principle Investigator or Sub/Co-Investigator	_____ Date