EP0031-101

IRB Approved Template
MUST BE APPROVED
FOR SITES BEFORE USE
Aug 16, 2022

INFORMED CONSENT DOCUMENT FOR RESEARCH

TITLE:	A Modular, Open-Label, Phase I/II Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of EP0031 in Patients with Advanced RET-altered Malignancies
PROTOCOL NO.:	EP0031-101 WCG IRB Protocol #20224030
SPONSOR:	Ellipses Pharma Limited
INVESTIGATOR:	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Phone Number Phone Number (24 hours) [24 hour number is required]

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

Key Information

This study is for research purposes, participation is voluntary

You are being asked to take part in a research study. Research studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.

Purpose, duration, overview of study

This study will investigate whether a new experimental treatment, EP0031, will be a safe and possibly effective treatment option for patients with *RET*-altered solid tumors. The study is designed to find a safe and effective dose of EP0031. EP0031 is an experimental drug, which means it has not been approved by the regulatory authorities.

The study drug is given in repeating 28-day periods called cycles. You will take EP0031 orally once per day of each 28-day cycle. During each cycle you will undergo tests and procedures. Most of these are part of regular care for your type of cancer. Some tests and procedures will be needed more often than normal because you are in this study. There will also be additional tests and procedures that are specific to this study to minimize risks and to provide information on how the study drug works on your tumor. Imaging of your tumor will be performed every 8 weeks during the first year of receiving study drug. You can continue to

receive EP0031 until your disease gets worse (unless otherwise decided by your study doctor), you experience unacceptable side effects, you withdraw your consent, or the study doctor believes you are no longer receiving benefit from the study drug. After you discontinue study drug, members of the study team will check on you every 3 months with a follow-up phone call to discuss the state of your disease and to find out what other treatment you are receiving after you stop taking the study drug.

Reasonable, foreseeable risks or discomforts

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your doctor may give you medicines to help lessen side effects. Many side effects may disappear soon after you stop taking EP0031. In some cases, side effects can be serious, long lasting, or may never go away.

EP0031 (or KL590586 as it is known in China) is currently under investigation in a Phase I/II trial (NCT05265091) in Chinese patients and as of March 2022, seven patients had received EP0031. Side effects assessed as related to EP0031 seen to date in this trial include:

- Increased heart rate (tachycardia)
- Heart palpitations
- Low levels of lymphocytes (a type of immune cell)
- Diarrhea
- Reduction in high-density lipoproteins (which can affect heart health)

Potential benefits

Taking part in this study may or may not make your health better. While doctors hope EP0031 will be an effective treatment against your type of cancer, this cannot be guaranteed.

We cannot promise that taking part in this study will help you, but the information we get from this study may help improve the treatment of other people with cancer in the future.

Alternatives to this research study

If you decide not to participate in this study, your other choices may include:

- Getting treatment or care for your cancer without being in a study;
- Taking part in another clinical study;
- Getting no treatment/getting palliative care.

Please note that as an alternative to participating in this study you may be able to receive treatment with another medicine, if recommended by your doctor, and if you have not received this type of treatment in the past. Other medicines may include multi-kinase inhibitors (e.g., vandetanib and cabozitinib if you have thyroid cancer) and medicines that selectively target RET-alterations (i.e., selpercatinib and pralsetinib).

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Patient Information Sheet

You are being invited to take part in a clinical trial. You have been diagnosed with a *RET*-altered solid tumor, and doctors at your hospital/clinic are working to develop better methods of diagnosis and treatment for this tumor. Your study doctor will explain the clinical study to you. Clinical studies include only people who choose to take part. In order to decide whether or not you want to take part in this clinical study, you should understand enough about its risks and benefits to make an informed decision. This process is known as informed consent. Please read the following information carefully, and discuss it with family, friends, and your primary physician if you wish. If you have any questions, you can ask your study doctor for more explanation.

1. Why is this study being done?

This study is designed to investigate whether the new experimental drug known as EP0031 will be a safe and effective treatment option for patients with *RET*-altered solid tumors. EP0031 is an experimental drug, which means it has not been approved by the regulatory authorities. The drug is therefore not available outside of this research study.

Approximately 265 patients will be enrolled in the study in about 30 sites in the US, UK and EU.

The study will start with a dose escalation part, during which increasing dose levels of EP0031 will be tested. The dose level which is found to be safe and tolerable during this phase of testing will then be used in the second part of the study (the dose expansion part). In the dose expansion part, we will continue to explore the safety and capacity of the body to tolerate the selected dose of EP0031, as well as looking at the effectiveness of this dose in different groups of patients.

Depending on when you join the study, you may participate in either the dose escalation or dose expansion part of the study. The dose you will receive will depend on the observations that have been made up to that time point. Your study doctor will be able to tell you the dose that you will receive.

2. Why have I been invited?

We are asking you to take part in this study because you have been diagnosed with a *RET*-altered solid tumor and you do not have access to or are not eligible for an approved selective RET inhibitor.

3. Do I have to take part?

No. You are free to decide whether or not to take part. If you decide to take part you will be asked to sign this consent form and be given this information sheet to keep. If you do decide to take part you will be free to leave the study at any time. You do not have to give a reason and it will not affect the standard of care you receive. If you decide not to take part, or you decide to leave the study, your doctor will discuss appropriate alternatives for your care with you.

4. What will happen to me if I decide to take part?

Participation in this research study will require a certain amount of commitment from you. You will be asked to visit the hospital/clinic frequently to receive study medication, to undergo tests and have blood samples taken. Hospital/clinic visits will sometimes take longer than normal visits for patients with your disease.

Before I begin the study:

Pre-screening:

To work out whether you are eligible for the study, we need to confirm your *RET* alteration status. If this is not already known, you may need to provide a blood or biopsy sample to be analyzed at a central location to confirm your *RET* status.

Screening

If you agree to take part in the study and have signed the consent form, you will be scheduled to come for a visit to make sure the study is right for you. During this visit, you will be asked about your medical history and general health including what medications you are taking. If you have a well-differentiated thyroid tumor, you must have received radioactive iodine before taking part in this study. Your vital signs will be measured (body temperature, blood pressure, breathing rate, and pulse). Routine blood tests will be taken and you will have a physical examination (including height and weight measurements). You will also undergo a full eye assessment, an evaluation of your heart function by echocardiogram (ECHO) or multigated acquisition scan (MUGA), and a recording of the electrical activity of the heart will be taken by electrocardiogram (ECG). A urine sample will be taken for analysis. A PCR-based or lateral-flow COVID test will be done (depending on the local requirements) and for women who are able to have children, a negative pregnancy blood test result must be confirmed before treatment can start. You will be asked about previous cancer treatments you have received. If you have received treatment at a cancer center other than the location of your study doctor, you will be asked to sign a records release form to allow the study doctor to confirm all previous treatment you have received for your disease.

A tumor biopsy will be taken (unless an archival tumor sample is available) and a CT or MRI scan will be done to assess your disease.

If you have had some of these tests recently, they may not need to be repeated. This will be decided by your study doctor.

We will monitor any side effects you may have from the time you start the study until 30 days after your last dose, and we will record any medications you are taking.

During the study:

If the examinations, tests, and procedures show that you can be in the study, you will enter the treatment period within 28 days of all screening activities. The treatment period starts on Cycle 1 Day 1 and a treatment cycle is defined as 28 days.

You will take EP0031 orally once per day of each 28-day cycle. However, if you are enrolled into the dose escalation part of the study, you may not need to take EP0031 on Day 2 of Cycle 1. Your study doctor will tell you if this is the case.

Your first dose of study medication will be taken in the clinic. If you are in the dose escalation phase, you will need to remain in hospital for up to 8 hours after your first dose for observation and blood sampling and if you are in the dose expansion part, you will need to remain in hospital for approximately 2 hours after your first dose.

You will take your other doses at home (aside from the days you are visiting the clinic). All doses should be taken on an empty stomach (at least 2 hours after the previous meal and 1 hour prior to the next meal) and at approximately the same time each day in the morning. Capsules should be swallowed whole, with water if necessary, and not chewed.

The total estimated blood volume to be taken will be approximately 275 mL in Cycle 1 (there are approximately 28 mL in an ounce, so this is about 10 ounces) and approximately 100 mL (about 3.5 ounces) in subsequent cycles during the first year of treatment. The total blood volume taken on any one day will not exceed 75 mL (about 2.5 ounces), except on Cycle 1 Day 1, when the blood volume will be approximately 135 mL (about 5 ounces).

Cycle 1 (visits on Days 1, 3, 8, 15 and 22 [and on Day 2 for some patients in the dose escalation part])

On Day 1 of Cycle 1, you will be asked about your general health, your vital signs will be measured (body temperature, blood pressure, breathing rate, and pulse), routine blood tests will be taken and you will have a physical examination (including weight measurement). An electrocardiogram will be done, a urine sample will be taken for analysis, and for women of childbearing potential, a negative urine pregnancy test result must be confirmed. Additional blood samples will be taken before and after the study drug is given to see what the body does to the drug (pharmacokinetics) and what the drug does to the body (pharmacodynamics).

During the early stages of the study, some patients (who progressed after treatment with a previous selective RET inhibitor) will be invited to provide a 'paired' tumor biopsy. One biopsy will be taken on Day 1 (or during the screening period), with another taken on or around Day 15 of Cycle 1. This is an exploratory part of the study which is optional and will help to identify the way that EP0031 acts upon your tumor.

On Day 2 of Cycle 1, patients in the dose escalation part of the study will have an additional blood sample taken for pharmacokinetic assessment.

Blood samples for pharmacokinetic assessments will be taken from all patients on Days 3, 8, 15 and 22 of Cycle 1 and on these days, you will need to remain in hospital for approximately 2 hours after dosing for this to be done. Additional blood samples will also be taken on Day 3, 8, and 15 to analyze potential clinical biological markers.

A brief physical examination and vital signs assessments will be repeated on Days 3, 8, 15 and 22 of Cycle 1, and your weight will also be recorded on Day 15 of Cycle 1. Routine blood tests and urine analysis will also be performed on Days 8, 15 and 22. An electrocardiogram will be done on Day 8 of Cycle 1.

You will be given a treatment diary to complete with all dosing information and any instances when you vomit or feel unwell in other areas. You will need to bring this diary together with all bottles (including empty ones) with you to all clinic visits and then return this diary at the end of the cycle, when you will receive a new one to complete.

Cycle 2 (visits on Days 1 and 15)

On Day 1 of Cycle 2, you will be asked about your general health, your vital signs will be measured (body temperature, blood pressure, breathing rate, and pulse), routine blood tests will be taken and you will have a physical examination (including weight measurement). You will also undergo a full eye assessment, an electrocardiogram will be done, a urine sample will be taken for analysis, and for women of childbearing potential, a negative pregnancy test result must be confirmed.

Additional blood samples will be taken for pharmacokinetic and pharmacodynamic assessments.

A brief physical examination, vital signs assessments, urine analysis, and routine blood tests will be repeated on Day 15 of Cycle 2.

On Day 1, you will be given a new treatment diary to complete. Please bring this diary and all bottles with you to all clinic visits.

Cycles 3-12 (visits on Days 1 and 15)

On Day 1 of Cycle 3 onwards, you will be asked about your general health, your vital signs will be measured (body temperature, blood pressure, breathing rate, and pulse), routine blood tests will be taken and you will have a physical examination (including weight measurement). An electrocardiogram will be done, a urine sample will be taken for analysis, and for women of childbearing potential, a negative pregnancy test result must be confirmed. You will also have a screening to check for any effects on your eyes, with a full eye assessment done if deemed necessary.

Additional blood samples will be taken for pharmacokinetic and pharmacodynamic assessments.

A CT or MRI scan will be repeated on Day 1 of every 2 cycles for up to 12 months (i.e., on Day 1 of Cycles 3, 5, 7, 9 and 11).

A brief physical examination, vital signs assessments, urine analysis, and routine blood tests will be repeated on Day 15 of Cycle 3 onwards.

On Day 1, you will be given a new treatment diary to complete. Please bring this diary and all bottles with you to all clinic visits.

Tumor response and safety follow-up visit (from 12 months onwards)

For as long as your disease does not get worse, we will ask you to attend follow-up visits every 3 months, where we will perform the following assessments:

- Recording of any side effects, other medications you are taking or new anti-cancer treatments
- Brief physical examination (including weight)
- Vital signs assessments (body temperature, blood pressure, breathing rate, and pulse)
- Blood sampling for pharmacokinetic and pharmacodynamic assessments
- CT or MRI scan

End of Treatment (EoT) Visits

EoT visit (7days post last dose)

Should you be withdrawn from the study for any of the reasons detailed in Section 6, you will need to attend an End of Treatment Visit within 7 days of your last dose of study drug, if possible. During this visit you will have the following assessments:

- Brief physical examination (including weight)
- Vital signs assessments (body temperature, blood pressure, breathing rate, and pulse)
- Recording of any side effects, other medications you are taking or new anti-cancer treatments
- Questions about your general health
- Electrocardiogram
- Routine blood tests
- Urine analysis
- Pregnancy test (for women of childbearing potential)
- Blood sampling for pharmacokinetic and pharmacodynamic assessments
- You may also undergo a CT or MRI scan
- You may be asked to provide another tumor biopsy, which will help characterize potential resistance mechanisms

EoT visit (30 days post last dose)

You will need to attend a post-treatment visit 30 days after your last dose. During this visit you will have the following assessments:

- Brief physical examination (including weight)
- Vital signs assessments (body temperature, blood pressure, breathing rate, and pulse)
- Recording of any side effects, other medications you are taking or new anti-cancer treatments
- Questions about your general health
- Electrocardiogram
- Routine blood tests
- Urine analysis
- Pregnancy test (for women of childbearing potential)
- Blood sampling for pharmacodynamic assessments

Long Term Follow-up Visits

Survival follow-up

If your disease gets worse after you have received EP0031, we would like to continue to keep track of your medical condition, until the end of the study is reached, or you withdraw consent. We will contact you by telephone every 3 months to see how you are doing and whether you have commenced any new anti-cancer treatment. If you have been into our clinic within 2 weeks of these times, we can use the date of these visits for your medical condition information.

5. What do I have to do?

You should contact the study nurse or doctor if you develop any side-effects or problems of any sort. If, for any reason you are not able to keep your appointment at the hospital for treatments or the necessary tests (e.g., blood tests, CT scans), then the treatment may have to be stopped. If this happens we will make arrangements for your care to continue.

You will need to take EP0031 every day and complete a Dosing Diary. You will be required to record the details of each EP0031 dose taken and return your completed diary on Days 8, 15, and 22 of Cycle 1 and on Days 1 and 15 of each subsequent cycle.

All study drug doses should be taken on an empty stomach (at least 2 hours after the previous meal and 1 hour prior to the next meal) and at approximately the same time each day in the morning. A normal, balanced diet is recommended, but grapefruit and grapefruit juice must be avoided.

Certain medicines (e.g. other cancer medicines) are prohibited during the study, because they can lead to misleading results in the study or potentially make EP0031 work in a different way. It is important that you tell your study doctor about all other medicines you are using on a regular basis, and if you change the dose of your medications or before you start a new one. Medications include herbal medications, prescription medicines and non-prescription (over the counter) medicines. Ask the study staff if you are in doubt if a medicine is important or not.

If you wear contact lenses, you must stop wearing these if you have any mild to moderate eye symptoms while receiving treatment with EP0031 until at least 1 week after symptoms have resolved. If symptoms recur, you must stop wearing your contact lenses until at least 1 week after treatment with EP0031 is permanently stopped.

If you are a male patient, you must agree not to father a child or donate sperm from enrolment through treatment and for 6 months following administration of the last dose of study drug. Women of childbearing potential must agree to use a highly effective method of contraception from screening until 3 months after the last dose of EP0031. Please read Section 8 of this information sheet and discuss with the study doctor which birth control methods to use.

If you are living with HIV, your doctor may need to modify your anti-retroviral treatment regimen to allow you to safely participate in this study.

6. How long will I be in the study?

You can continue to receive EP0031 until your disease gets worse (unless otherwise decided by your study doctor), you experience unacceptable side effects, you withdraw your consent, or the study doctor believes you are no longer receiving benefit from the study drug. You may therefore receive EP0031 for up to 4 years within this study. If your doctor decides you can continue to receive EP0031 after your disease gets worse, you will be given a new informed consent form, which will explain your other treatment options. The study will end after the last patient has taken EP0031 for 12 months or 30 days after the final patient discontinues treatment. EP0031 will not be available after the end of the study.

We would like to keep track of your medical condition until the end of the study. We will contact you by telephone every 3 months or check your medical records with us (if within 2 weeks of every 3 months) to see how you are doing. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study drug.

7. Can I stop being in the study?

You can decide to stop at any time. It is important to tell your study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. It may be necessary for you to have certain tests or procedures if you decide to stop, to ensure your safety (as described in Section 4). Your doctor will discuss with you what follow-up care and testing could be most helpful to you.

Your study doctor may stop you from taking part in this study at any time if he or she believes it is in your best interests, or if you do not follow the study rules, or if the study is stopped.

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

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your doctor may give you medicines to help lessen side effects. Many side effects disappear soon after you stop taking EP0031. In some cases, side effects can be serious, long lasting, or may never go away.

EP0031 (or KL590586 as it is known in China) is currently under investigation in a Phase I/II trial (identified as "NCT05265091" on the ClinicalTrials.gov website) in Chinese patients and as of March 2022, seven patients had received EP0031. Side effects assessed as related to EP0031 seen to date in this trial include:

- Increased heart rate (tachycardia)
- Heart palpitations
- Low levels of lymphocytes (a type of immune cell)
- Diarrhea
- Reduction in high-density lipoproteins (which can affect heart health)

Due to the small amount of clinical data for EP0031, potential risks of EP0031 are based on animal studies, pharmacodynamic studies, and research on similar drugs.

QTc prolongation

A heart rhythm disorder that can cause fast, chaotic heartbeats. The rapid heartbeats may cause sudden fainting. As a precaution, if you have any abnormalities in heart rhythm, conduction, or morphology on your electrocardiogram, you will not be able to take part in the study. Electrocardiograms are also performed regularly throughout the study.

Other cardiac effects

Other effects on the heart have been seen in animal studies, therefore, if you have heart disease or a history of heart attacks or chest pain, you will not be able to take part in the study.

Respiratory effects

Mineral build up in the lungs has been observed in animal studies, so effects on the respiratory system will be monitored through reporting of side effects.

Gastrointestinal effects

Muscle wastage of the gullet (esophagus) has been observed in animal studies, so upper and lower gastrointestinal effects will be monitored through reporting of side effects.

Eye cell surface effects

Breakdown of the cells of the eye has been observed in animal studies. You will therefore need to undergo a full eye examination prior to starting this study and undergo repeat eye assessments throughout the study as needed.

Reproductive organ effects

Male patients

Male fertility (sperm production) may potentially be compromised by EP0031 and it is not yet known if this is reversible. Therefore, if you are male, you will be advised to arrange for the freezing of sperm samples prior to the start of the study.

You should not father children or donate sperm during the study and for 6 months after your last dose. If your partner is of childbearing potential, this may be by you using a condom or by your partner using highly effective contraception (see definition below).

Female patients

If you are pregnant or breast feeding you may not take part in this study.

Women of childbearing potential must have a negative pregnancy test prior to starting the study and have repeat pregnancy tests during the study. If you become pregnant or think you may be pregnant while on the study, you must notify your study doctor immediately and study drug administration will be stopped.

Women of childbearing potential must use a highly effective method of contraception from screening until 3 months after the last dose of EP0031, defined as one of the following:

- True abstinence (not periodic abstinence or withdrawal)
- Sterilization (surgical bilateral oophorectomy with or without hysterectomy or tubal ligation at least 6 weeks before starting study drug)
- Vasectomized partner (at least 6 months prior to screening)
- Placement of an intrauterine device (IUD) or intrauterine system (IUS).
- Hormonal implants or combined oral contraceptives
- In addition, male partners of patients of childbearing potential using hormonal contraception must use a condom until 2 months after the last dose of EP0031.

Hematopoietic effects

Effects on the thymus and spleen (organs in the body which produce immune cells) have been observed in animal studies. Therefore, if you have low immune cell counts, you will not be able to take part in the study. Immune cells will also be monitored regularly throughout the study through routine blood tests.

Kidney effects

Reversible kidney damage has been observed in animal studies. If you have kidney inflammation or have had a kidney transplant, or have insufficient renal function, you will not be able to take part in the study. Kidney function will be assessed before you may start on study treatment and throughout the study.

Musculoskeletal effects

Effects on bones and joints has been observed in animal studies, so this will be monitored through reporting of side effects.

Liver effects

Elevated liver function tests have been observed in animal studies, indicating possible liver damage. You will undergo regular monitoring of liver function tests and you should report any side effects associated with liver toxicity, such as, nausea/vomiting, weight loss, abdominal pain/tenderness, feeling tired, bleeding/easy bruising, yellowing of the eyes, skin and urine, fever, and rash.

Tumor lysis syndrome

Tumor lysis syndrome occurs when more chemicals and substances are released during cell breakdown than the body can deal with. This can be an emergency condition. It has been observed in patients with thyroid cancer who received a similar drug to EP0031.

You should report any signs or symptoms of this, such as nausea, vomiting, feeling tired, swelling of tissues, shortness of breath, muscle cramps, or seizures.

Other possible effects

Because of the way EP0031 works, potential side effects associated with this include, high blood pressure, wound healing complications, blood clots, protein in your urine, bleeding, and headache, seizures, altered mental status and visual loss.

Risks from study procedures

Risks from tumor imaging (CT or MRI scan)

You will be required to undergo CT or MRI scans, approx. every 8 weeks. Leaflets will be available providing more information on these scans.

During the first year of receiving study drug, you will have CT scans every eight weeks. Most patients will have CT scans of the chest and abdomen. During this year, your total ionizing radiation exposure due to the study would be about 128 mSv. For most patients, this would be about 54 mSv more radiation than required for standard of care. To put that in context, everyone is exposed to background radiation of about 3 mSv per year from natural sources like cosmic rays and soil. After the first year of treatment, scans will become no more frequent than would be required per standard of care.

Often contrast medium is injected prior to a CT scan. This is like a dye and will spread through your body and will help give clearer images of your cancer. The contrast medium will be injected into a vein, which may cause some discomfort and bruising. There is a risk of potentially serious allergic reactions in some individuals who receive contrast medium.

Similar to the CT scan, a contrast solution may also be injected into your vein before the MRI is done. The risks associated with the MRI contrast agent include mild nausea, headache, hives and temporary low blood pressure, although such reactions are rare.

An MRI does not use X-ray radiation, but strong magnets. You therefore cannot have any metal implants in your body for an MRI scan. It also takes a little longer than a CT-scan. For most participants the risks or side effects associated with undergoing MRI are minimal. If applicable, you will be asked questions to make sure you can safely have an MRI scan. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed.

For further specific information about any of the procedures in this study, please ask your study doctor and/or the specialist doctor (radiologist) who will perform some of these procedures.

Electrocardiogram

An electrocardiogram (ECG) is a standard cardiac examination in which the electrical activity of your heart is recorded. The method is purely external, but removal of the electrodes may cause temporary skin irritation and discomfort in the chest region.

Echocardiogram (ECHO) or Multigated Acquisition (MUGA) Scan

An ECHO is a non-invasive ultrasound imaging test which carries little to no risk. You may experience discomfort from the positioning of the imaging device because it can put pressure on the surface of the body.

During a MUGA scan, images will be taken of the beating heart to see how well your heart is pumping blood. It will be done using a radioactive tracer which will be injected through a needle placed in a vein of your arm. You will be provided with personalized instructions by your study doctor on how to prepare for a MUGA scan. The MUGA scan also contributes a small radiation dose to the total in this study (6 mSv, similar to 2 years of radiation that we typically receive from background sources). The radiology staff will check you closely for an allergic reaction, which is rare but could be life-threatening. There is a chance that you may experience discomfort, pain, and/or swelling at the injection site and, as is the case with any injection, there is an increased risk of infection at the injection site.

Risks from tumor biopsies

In this study you will be required to undergo biopsies (if you have a safely accessible site), which may be painful. If you choose to provide a 'paired' tumor biopsy, then you will need to undergo a total of three biopsies during the study (this part of the study is optional). Local anesthetics will be used, according to practice, at your hospital. The biopsies may also cause a little local bruising but this should be mild and easily controlled with pressure over the area. In addition to using ionizing radiation for your CT scans, the biopsies for this study may also be taken using X-ray or CT guidance to assist your clinicians. Your doctor will explain more about the specific risks associated with the biopsies, once the specific cancer lesion has been selected for a biopsy.

Risk from blood sampling

The most common risks associated with taking blood samples from the arm include pain where the needle is introduced, bruising, and light-headedness and on rare occasions, infections.

9. Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope EP0031 will be an effective treatment against your type of cancer, this cannot be guaranteed.

We cannot promise that taking part in this study will help you, but the information we get from this study may help improve the treatment of other people with cancer in the future.

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

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment/getting palliative care

Please note that as an alternative to participating in this study you may be able to receive treatment with another medicine, if recommended by your doctor, and if you have not received this type of treatment in the past. Other medicines may include multi-kinase inhibitors (e.g., vandetanib and cabozitinib if you have thyroid cancer) and medicines that selectively target RET-alterations (i.e., selpercatinib and pralsetinib).

Your study doctor will discuss your choices, and their risks and benefits, with you before you decide if you will take part in this study.

11. What if new information becomes available?

Sometimes, during the course of a research project, new information becomes available on the drug that is being studied. If this happens, your doctor will tell you about it and discuss with you whether you want to stay on the study. If you decide to stop, you should tell your study doctor and he or she will arrange for your care to continue. If you decide to stay on the study, you may be asked to sign an updated informed consent form.

On receiving new information, your study doctor might think it is in your best interests to stop your participation in the study. If so, he or she will explain the reasons for his or her decision and arrange for your care to continue.

12. Will my medical information be kept confidential?

If you agree, your primary physician will be told that you are taking part in this study.

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What information may be used and given to others?

If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health including:

- Medical and research records (which may include dates of birth, death, admissions, social security number)
- Records about phone calls
- Records about your study visits
- Records of physical exams
- Laboratory, x-ray, and other test results
- Records about study medications
- Records about any study drug you received

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

Your information may be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor.

For this study, "sponsor" also includes:

- Theradex Oncology, an agent for the sponsor

Information about you and your health which might identify you may be given to:

- Your Insurance Company
- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Regulatory authorities in other countries
- Regulatory authorities to whom certain diseases (reportable diseases) must be reported
- WCG IRB

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site or accessing your medical records remotely. They will follow how the study is done, and they will be reviewing your information for this purpose.

The information may be given to the FDA. It may also be given to regulatory authorities in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of regulatory authorities.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

WCG IRB may review the information. The IRB is a group of people who perform independent review of research as required by regulations.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others, if this is necessary to ensure the reliability of the research. You understand that the revocation will not apply to your insurance company when the law provides your insurance company with the right to contest a claim under your policy.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission. Your personal information may be disclosed if required by law.

Your records for this study may be sent by facsimile transmission (FAX machine) or over the Internet. It is possible that your records could be sent to the wrong person, although every effort will be made to avoid this.

Expiration of Authorization

Unless otherwise revoked, this authorization will not expire.

13. What will happen to any samples I give?

We will collect blood, urine and tumor tissue (biopsy) samples in this study, as described in Section 4.

The blood and urine samples that are taken for safety testing will be analyzed by hospital staff and at the hospital's own laboratory. However, other samples are sent to be analyzed at different laboratories.

Some of the blood samples and tumor biopsy samples will be sent to and stored at global central laboratories for up to 15 years from the end of study, for additional testing to understand the cancer, the drug response or to validate diagnostic or exploratory biological marker tests. These are secure facilities, requiring international security and safety standards for laboratories. After the 15 years of storage, the samples and any parts of them used for analyses will be destroyed.

Special precautions are taken to ensure that the research in this study will be carried out with a very high degree of confidentiality. Your samples will be labeled with the same code that is given to you in the main study, but not with personal identifiers such as your name.

14. Will any genetic tests be done?

You will have blood samples and tumor tissue samples taken during the study which may be analyzed using genome sequencing such as whole genome sequencing or whole exome sequencing. This means we will map part of your genetic code. The results will be used to find genetic mutations that help to predict response to the study drug EP0031 (e.g., efficacy, resistance or rapid progression, development of adverse events) and to increase understanding and knowledge of the disease biology. The collection of these genetic samples for whole genome sequencing or whole exome sequencing is optional. The results may be reported independently of this study. You will not be named in any report.

15. What will happen to the results of this study?

When all the data has been collected and analyzed, a final report will be written and published on the study. You will not be identified in reports or publications. The study doctor will receive a report of the study results. You can contact the study doctor and obtain a copy of the results. You can also decline to learn the results if you so wish.

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.

16. Who is organizing and funding this study?

This study is being organized and funded by Ellipses Pharma, who will supply the study drug EP0031. Their address is: 10 Stratton Street, London, W1J 8LG, UK. The doctors conducting the study are not being paid, but a payment will be made to the hospital to cover the cost of the study tests and procedures. Your study doctor will tell you if he or she has any financial or other ties with Ellipses Pharma.

17. What are the costs of taking part in this study?

You will not have to pay for the costs of the study drug. However, you and/or your health plan or insurance company may need to pay for some or all of the other costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Website at: http://cancer.gov/clinicaltrials/understanding/insurance-coverage.

You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Website.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

You will not be paid for being in this study.

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

It is important that you tell your study doctor, [insert investigator's name], if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him or her on telephone number [insert telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study has no plans to pay for medical treatment.

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

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

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

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

20. Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, [Doctor's name] at [Doctor's telephone number] (24 hours).

[IF APPLICABLE: Or you may contact your study nurse [Nurse's name(s)] at [Nurse's telephone number(s)].]

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

EP0031-101

IRB Approved Template
MUST BE APPROVED
FOR SITES BEFORE USE
Aug 16, 2022

CONSENT FORM FOR CLINICAL RESEARCH

A modular, open-label, phase I/II study to evaluate the safety, tolerability, pharmacokinetics and efficacy of EP0031 in patients with advanced RET altered malignancies

Patient Statement

I, the undersigned, have been told about this research study. I have been informed about the procedures to be followed, the possible risks and the benefits that I may experience as a result of my taking part. I have read the description of this research (or had it translated into a language I understand) and had the time and opportunity to ask questions and to decide whether or not to take part. I understand that my participation is voluntary and that I may withdraw from the study at any time without penalty or loss of any benefits I may otherwise be entitled to. I agree to take part in this research study.

I understand that any of my medical records may be inspected by Ellipses Pharma, and their representatives, or by WCG IRB, or by people from the hospital's IRB or by national regulatory authorities to check that the study is being carried out correctly. I give permission for these parties to have access to my medical records. I give permission for my physician to be notified in writing of my participation in this study. I consent to the use of my samples for the research as described above.

I understand that providing paired tumor biopsy samples and samples for genetic testing is optional within this study and that if I provide these samples, I consent to the use of my samples for the research as described above. Please indicate if you consent to these optional samples by marking 'YES' or 'NO' in the corresponding boxes below. You will still be able to take part in the study if you do not provide consent for these optional samples.

I consent to the optional 'paired' tumor biopsy samples: YES ☐ NO ☐

I consent to the optional samples for genetic testing: YES ☐ NO ☐

I may contact Dr [investigator's name] at any time with questions about this study.

I will be given a signed and dated copy of the patient information sheet and consent form.

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person Conducting Informed Consent Discussion	Date	Signature

One copy for patient; one copy for investigator; one copy to be kept with hospital notes.

****For Sites in California****

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?

The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

Who might get this information?

The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2070.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Authorization:
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

Signature of Subject **Date**