Study title:
Single-arm Study With Bimiralisib in Patients With HNSCC Harboring NOTCH1 Loss of Function Mutations

ClinicalTrials.gov record number:
NCT03740100

MD Anderson protocol number:
2018-1003

PIQUR number:
PQR309-009

Document:
Informed Consent Document

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Cover page (14 pages total)

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Open-label, single arm, two-stage study, evaluating the efficacy and safety of bimiralisib in patients with recurrent or metastatic head and neck squamous cell carcinomas (HNSCC) harboring NOTCH1 loss of function (LOF) mutations
2018-1003

Subtitle: PQR309-009_Protocol v.5, Amendment 4 – ICF v.8, dated 28April2020

Study Chair: Faye M. Johnson

Participant's Name _____ Medical Record Number _____

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to learn if bimiralisib can help to control HNSCC that has a NOTCH1 LOF mutation and is either refractory (has not responded to treatment) or metastatic (has spread). The safety of this drug will also be studied.

This is an investigational study. Bimiralisib is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can explain how the study drug is designed to work.

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may continue taking the study drug for as long as the doctor thinks it is in your best interest.

Bimiralisib will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard treatments for the disease, such as other drugs, surgery, or radiation therapy. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. You will have screening tests to help the doctor decide if you are eligible:

- You will have a physical exam.
- Previously collected information (such as genetic information and other information about mutations) about the tumor will be reviewed.
- You will have an EKG to check your heart function.
- Blood (about 4 teaspoons) will be drawn for routine tests. You will need to fast (not eat or drink anything except water) for 10 hours before these blood samples are drawn. If you can become pregnant, this routine blood draw will also include a pregnancy test. To take part in this study, you must not be pregnant.
- If you are a post-menopausal woman, blood (about 1 teaspoon) will be drawn for hormone testing to confirm that you are post-menopausal.
- Urine will be collected to make sure you are not a smoker.
- You will have a CT scan or MRI to check the status of the disease.
- If it is available, tumor tissue removed during a previous procedure may be collected to check protein levels related to your NOTCH1 mutation.
- You will complete 2 questionnaires about your mood. This should take about 15 minutes to complete.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Up to 35 participants will be enrolled in this study. Most if not all of these patients will take part at MD Anderson, although 1-3 other sites may be added.

Study Drug Administration

If you are found to be eligible to take part in this study, you will take bimiralisib capsules by mouth at about the same time in the morning on an empty stomach (at least 1 hour before breakfast) with a full cup (about 8 ounces) of still water. You will take the capsules on 2 days of each week while you are on study (2 days taking the drug, followed by 5 days of no drug each week). Capsules must be swallowed whole.

Do not bite or chew on the capsules. If the capsule breaks in your mouth, take additional water and rinse.

If you are unable to swallow bimiralisib capsules, your study doctor will instruct you on how to prepare a suspension of bimiralisib. A separate leaflet will be handed out to you by your study doctor. You will be asked to open the capsules and suspend their contents – white pellets – into water which you can either swallow as a suspension or administer through a feeding tube. The study team will go through this procedure with you step by step so that you – or your caregiver – can repeat it at home. Contact your study doctor for questions.

If you have any severe side effects, the dose of the study drug you receive may be changed.

You will be given a diary to take home with you to write down the dates, times, and the amount of the study drug you take. You should also confirm that you took your dose of bimiralisib on an empty stomach and if you missed any doses of bimiralisib.

You must return all unused capsules and the diary as often as defined by your physician.

You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, if you become pregnant, if you no longer want to take part, or if you are unable to follow study directions.

If you discontinue study treatment, you will come for the end-of-treatment visit within 7 days of the decision to discontinue.

Study Visits

You will need to fast for 10 hours before each visit. **On visit days, you will take bimiralisib in the clinic**. Do not take the study drug before the visit.

The day before starting your treatment, blood (about 2 teaspoons) will be drawn for routine tests.

You will then have study visits on **Days 1, 8, 15, 22, 43, 64, 85, and every 6 weeks after that.** At each visit:

- Blood (about 4 teaspoons) will be drawn for routine tests.
- You will complete 2 questionnaires about your mood (except at Day 1).

In addition, some study tests will only be performed at certain visits:

- On Day 1, 8, 22, 43, 64 and 85, blood (about 1 teaspoon each time) will be drawn for pharmacokinetic (PK) testing before the morning dose and then once within 1-3 hours after the dose before you eat anything.
- At Days 43, 64, 85, and every 6 weeks after that, if you can become pregnant, you will have a urine or blood pregnancy test.

- At Days 43, 85, and every 6 weeks after that, you will have a CT scan or MRI to check the status of the disease

End-of-Treatment Visit

After you stop taking the study drug:

- You will have a physical exam.
- You will have an EKG.
- Blood (about 4 teaspoons) will be drawn for routine tests. If you can become pregnant, this routine blood draw will also include a pregnancy test
- You will have a CT scan or MRI to check the status of the disease
- You will complete the mood questionnaires.

Follow-Up

About 30 days after your last dose of study drug, you will either come back for a visit or a member of the study staff will call you to find out how you are doing, if you are having any side effects, and if you have started or stopped any medications. This visit/call may last up to 30 minutes.

Other Instructions

- COVID-19 ("Coronavirus disease 2019") is a respiratory disease caused by a novel coronavirus ("SARS-CoV-2") that was initially detected in China in late 2019 but has spread around the world, including across the United States. MD Anderson has taken additional actions to prevent the introduction or spread of COVID-19 in patients. The study doctor will give you more instructions about this.
- You must come to every study visit so that the study doctor can monitor your health condition while taking part in the study. If you have to miss at least 2 study visits due to COVID-19, you will be taken off study.
- During the study, you cannot receive any other cancer treatments.
- During the study, you cannot receive pantoprazole, omeprazole or any other proton pump inhibitor drugs because these drugs would substantially decrease the levels of bimiralisib in your body. Uncontrolled use of H2 antagonists (such as Ranitidine, famotidine, cimetidine, nizatidine, roxatidine, lafutidine, and so on) and direct antacids (such as Maalox, Tums, mylox, Rolaids, and so on) are prohibited for the same reason. However, if you need medication to lower the acidity of your stomach, you may take up to 300mg of ranitidine every day at bedtime. If you do this, you will take bimiralisib in the early evening. The study doctor will give you more instructions about this.
- It is not known what side effects may occur if bimiralisib and other drugs are given in combination. Be sure to tell your study doctor about all prescription and/or over-the-counter drugs, vitamins, herbal drugs, and nutritional supplements you are taking or will take.
- While taking part in this study, you must not take part in any other research study.
- While taking part in this study, you must refrain from tobacco smoking and e-cigarette use ("vaping") because both tobacco smoking and "vaping" would substantially decrease the levels of bimiralisib in your body.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after the drug is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving the drug. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Bimiralisib Side Effects

This is an early study of bimiralisib, so the side effects are not well known. Based on early human studies, bimiralisib may cause the following side effects:

• fatigue • depression • mood swings • high blood sugar (possible diabetes) • agitation • dry skin/itching • skin rash	• loss of appetite/weight loss • diarrhea • vomiting/nausea • constipation • abdominal pain • upset stomach	• abnormal liver tests (possible liver damage) • pneumonitis (lung inflammation) • weakness

Bimiralisib may cause a low blood cell count (red and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Based on similar drugs, bimiralisib may cause:

• difficulty sleeping	• suicide attempts	• psychosis (loss of contact with reality)

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

EKGs may cause discomfort as EKG pads may cause skin irritation.

Fasting may cause your blood sugar to drop. You may feel tired, hungry, and/or nauseous. If you have diabetes, it is important to talk to your doctor about managing your blood sugar while fasting.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, you must use an effective method of birth control while on study and for at least 90 days after your last dose of study drug. Effective methods include:

- Intrauterine device (IUD) or intrauterine system (IUS) in combination with condoms or occlusive cap with spermicidal foam/gel/film/cream/vaginal suppository
- Males must always use a condom while on study, even if they have had a vasectomy. Female partners of male participants must also use an effective form of birth control listed here.
- Sterilization of you or your partner

You may not use birth control pills or other hormonal methods of birth control (such as injections) while on study.

Males: Do not donate sperm while you are on study and for at least 90 days after your last dose of study drug. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, you will have a full skin exam performed by a dermatologist at Screening. This is being done to see if the study drug may help to treat specific skin lesions. If you are found to have one of these lesions, you will then continue to have these skin exams every 6 weeks while you are on study. The dermatologist will discuss treatment options with you which will be performed

outside of this study. The skin monitoring during your participation in this study will not interfere with any standard of care treatment that you may need for potential skin conditions.

Optional Procedure #2: If you agree, additional blood (about 4 teaspoons) will be drawn for circulating DNA (ctDNA) testing at screening, on Day 43, and then at the end-of-treatment visit. ctDNA testing helps researchers learn more about the genetic information of the disease and may help to understand why the disease may or may not respond to treatment with drugs like bimiralisib.

There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure Risks:

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. Genetic research in this study will be strictly limited to the tumor, similar to the analyses that were performed to characterize your tumor in the first place. Like the results from the earlier genetic analyses prior to your study participation, the results of this study-specific ctDNA testing may be put in your health records.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have skin exams to check for certain lesions that may be affected by the study drug?

YES **NO**

Optional Procedure #2: Do you agree to have additional blood draws for ctDNA testing?

YES **NO**

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or PIQUR Therapeutics AG for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for your participation in this study. In addition, you will not receive financial reward from any patents or discoveries that result from this research.

You may be reimbursed up to $50 per study visit for meals and parking. You will be asked to provide receipts for expenses to be eligible for reimbursement. In case you will be traveling between 50 and 250 miles, you will be reimbursed at $ 0.50 per mile up to $250 for transportation expenses and up to $150 hotel expense per Study Visit. In case you travel more than 250 miles for your hospital visit, you will be reimbursed up to $350 for airfare expenses and up to $150 hotel expense for Study Visit. You will be asked to provide receipts for expenses to be eligible for reimbursement.

Please ask the study staff for details.

Additional Information

4. You may ask the study chair (Dr. Faye M. Johnson, at 713-792-6363) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, PIQUR Therapeutics AG, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: PIQUR Therapeutics AG.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- PIQUR Therapeutics AG, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Precision Oncology, PRA Health Services, and Advyzom and WIL
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

For PK testing, your de-identified blood samples will be sent to Charles River Laboratory (CRL).

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2018-1003.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

NAME OF TRANSLATOR _____ SIGNATURE OF TRANSLATOR _____ DATE _____

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) _____ DATE _____

PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION _____