MC1152

A Phase II Efficacy Trial of Pazopanib in Non-Clear Cell Metastatic Renal Cell Cancer (mRCC) PINC

NCT01767636

Document Date: 08/01/2018

MAYO CLINIC

Name and Clinic Number

Approval Date: **August 1, 2018**
Not to be used after: **February 21, 2019**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1152**,** A Phase II Efficacy Trial of Pazopanib in Non-Clear Cell Metastatic Renal Cell Cancer (mRCC) (PINCR)

IRB#: 11-003340

Principal Investigator: Dr. B. Costello and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you a copy of this form to keep.

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CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigators: Dr. Brian Costello (Rochester) **Other Study Contacts:** Dr. Thai H. Ho (Arizona) Dr. Winston Tan (Florida)	**Phone:** (507) 284-2511 (480) 301-8000 (904) 953-7290 **Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Subject Advocate **(The RSA is independent of the Study Team)**	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchsubjectadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information
Research Billing	**Rochester, MN:** (507) 266-5670 **Florida:** (904) 953-7058 **Arizona:** (800) 603-0558	▪ Billing or insurance related to this research study

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Other Information:

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

1. Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have been diagnosed with metastatic non-clear renal cell cancer.

2. Why is this research study being done?

The purpose of this study is to determine how the study drug pazopanib works in the treatment of metastatic non-clear cell renal cell cancer and disease progression. The use of pazopanib for this indication in the study is considered investigational, which means it has either not been approved by the Food and Drug Administration (FDA) for routine clinical use or for the use described in this study. However, the FDA has allowed the use of this drug in this research study.

3. Information you should know

Who is Funding the Study?

Novartis is funding the study and will pay the institution to cover costs related to running the study.

Information Regarding Conflict of Interest:

One or more of the investigators associated with this project have a financial interest in one of the companies sponsoring this trial and/or providing a product for this trial and that the investigator may stand to gain financially from the successful outcome of the research.

Both the Mayo Clinic Conflict of Interest Review Board and the Institutional Review Board have reviewed the financial interest for one or more of the investigators and/or Mayo Clinic related to this research and they have determined that this financial interest poses no additional significant risk to the welfare of participants in this research project or to the integrity of the research.

Additional information is available to any interested study participant regarding the details of this financial interest and how it is being managed by contacting the study coordinator or the Office of Conflict of Interest Review at 507-284-0075.

4. How long will you be in this research study?

You will be in the study for 3 years or until your disease gets worse.

5. What will happen to you while you are in this research study?

If you agree to be in the study, you will be asked to participate in the following:

On your first visit, you will have tests done to evaluate your condition and ability to participate in the study. These include blood tests, 24 hour urine sample, echocardiogram (a test which looks at your heart and surrounding tissue), thyroid function test, CT (x-ray) or MRI of the head, electrocardiogram (EKG – a test to measure your heart function), and CT (x-ray) or MRI scan of chest, abdomen or pelvis. Your doctor will ask you questions about your medical history and examine you. If you are a woman who can have children, you will be required to have a negative pregnancy test within 7 days prior to starting the study. The pregnancy tests must be negative for you to start treatment.

We will collect tissue samples from a previous biopsy you have had for testing.

For the bone scan, a small amount of radioactive material will be injected in your vein and a special camera will be used to image the material inside of your body.

If you are eligible and agree to participate, you will begin treatment. You will receive pazopanib tablets once a day, every day that you are on the study.

Pazopanib should be taken orally without food at least one hour before or two hours after a meal. The tablets should be swallowed whole and must not be crushed or broken. The time of day the tablets are taken should be relatively constant.

You will also be asked to keep a diary to record your medications taken. This should take no more than a couple of minutes a day to complete.

If your disease gets worse, you will be taken off treatment with the study drug and your physician may start you on another treatment. We will continue to collect information about how you and your disease are doing for up to 3 years after you stop treatment.

If your disease gets better, you will continue on the study for up to 12 more cycles (months). After this you will go to event monitoring and we will continue to collect information about how you and your disease are doing for an additional 2 years.

You will be watched for side effects and the dose will be adjusted if necessary. If your dose is reduced, you will continue on with the same treatment schedule as before.

These are the procedures and study visits:

Before study enrollment	• Sign informed consent • History and exam • Vital signs including temperature • Routine blood test (including complete blood count) • Pregnancy test at least 7 days prior to registration (only for females who may still become pregnant) • Urinalysis • Thyroid function test • Blood coagulation test • CT/MRI scan of the head • Echocardiogram • EKG • CT/MRI scan of chest, abdomen or pelvis
Prior to each new cycle	• History and exam • Vital signs including temperature • Check for side effects • Routine blood tests (including complete blood count). Can be drawn at outside institution • Blood coagulation test • EKG

Weeks 2, 6 and 10	• Routine Blood tests
Every other cycle	• Thyroid function test • CT/MRI scan of chest, abdomen, or pelvis • Bone scan (if applicable) • Echocardiogram (every four months)
End of Treatment	• History and exam • Vital signs including temperature • Routine blood tests (including complete blood count)

The schedule of blood specimen tests is listed above. Approximately 2 tablespoons of blood will be drawn at each time.

For the time you are enrolled in this study, you may not donate blood, or participate in other cancer research trials or other trials with new medications.

6. What are the possible risks or discomforts from being in this research study?

GW786034 (Pazopanib)

Likely risks of GW786034 *(events occurring greater than 20% of the time)*

- Feeling tired (Fatigue)
- Loss of appetite, not feeling hungry (Anorexia)
- Loose stools (Diarrhea)
- Feeling sick to your stomach (Nausea)
- Throwing up (Vomiting)
- High blood pressure (Hypertension)
- Decreased function of the thyroid gland and/or thyroid hormone, which can result in feeling tired and weight gain, that may first show up as an increased levels of thyroid stimulating hormone (Hypothyroidism)
- Loss of pigment in the skin causing it to look lighter (Skin de-pigmentation)
- Loss of hair color
- Abnormal liver function tests which may indicate that your liver is not functioning properly or injured
- Abdominal pain
- Headache
- Tumor pain

Less likely risks of GW786034 *(events occurring less than or equal to 20% of the time)*

- Hair thinning or loss (Alopecia)
- Loss of the protein in the urine (Proteinuria)
- Decrease in red blood cells, which are the oxygen carrying cells, which could make you feel tired (Anemia)
- Opening or hole in the bowel that can lead to infection, may require surgery to repair and/or lead to death (Bowel perforation)
- Fever (Pyrexia)
- Flare of diverticulitis (inflammation of the bowel associated with diverticulosis of the colon)
- Inflammation of the colon (Colitis)
- Rash/flaking or shedding of outer layer of skin
- Nose bleed (Epistaxis)
- Bleeding from the lungs or respiratory tract (Pulmonary hemorrhage)
- Sensation of lightheadedness or vertigo (Dizziness)
- Joint pain (Arthralgia)
- Decrease in the number of white blood cells, which are the infection fighting cells and important to the immune system, which could put you at risk for infection (Neutropenia, Lymphopenia, Leukopenia)
- Decreased number of blood cells (platelets) that help to clot the blood (which could put you at increased risk of bleeding) (Thrombocytopenia)
- Difficulty passing stool (Constipation)
- Intestinal gas (Flatulence)
- Change in taste sensation (Dysgeusia)
- Restless movements caused by abnormalities in the part of the brain that coordinates movement
- Coughing up blood or blood tinged sputum (Hemoptysis)
- Anxiety, agitation, confusion
- Feeling sad or blue (Depression)
- Abnormal blood level of fat-digesting enzyme (lipase) and/or abnormal digestive enzyme level (amylase) potentially indicating inflammation or injury to the pancreas
- Cough
- Low levels of magnesium in the blood (Hypomagnesmia)
- Decreased level of phosphorus in the blood (Hypophosphatemia)
- Excessive or abnormal loss of body fluids (Dehydration)
- Elevation of a liver pigment (bilirubin) in the blood indicating liver dysfunction (Hyperbilirubinemia)
- High blood sugar (Hyperglycemia)
- Increased magnesium in the blood (Hypermagnesemia)
- Low blood sugar (Hypoglycemia)
- Muscle pain (Myalgia)

- Shortness of breath or difficulty breathing (Dyspnea)
- Weight loss
- Pain, redness or tissue breakdown at the sites where there has been exposure to radiation therapy (Radiation recall)
- An increase in the amount of time it takes to "recharge" heart cells after they have been stimulated to beat. This increase in time can cause an abnormal heartbeat that can cause you to "pass-out or faint" and/or be life threatening (QT prolongation)
- Indigestion or heartburn (Dyspepsia)
- Infections, including lung infection (pneumonia)
- Insomnia (difficulty sleeping)

Rare but serious risks of GW786034 *(events occurring less than 2-3% of the time)*

- Collection of fluid in the space around the lung (Pleural effusion)
- Decrease in the ability of the heart to pump blood, because of weakening of the heart muscle (Congestive heart failure)
- Development of fluid in the area around the heart (Pericardial effusion)
- Abnormal heartbeat (Arrhythmia)
- Bleeding in the brain (Cerebral hemorrhage)
- Blood clot in a vein (Deep vein thrombosis)
- Blood clots in the lungs which could be life threatening or cause death (Pulmonary embolism)
- Lack of oxygen to the heart muscle which can cause damage to the heart (Heart attack)
- Kidney injury (Kidney failure)
- Elevated liver enzymes
- Cough and/or a sudden spasm of the vocal cords which may result in the closing of the airway (Laryngospasm)
- Abnormal connection between different parts of the body (fistula)- This can occur in the between structures of the urinary tract (i.e. bladder) and the genital or reproductive system (i.e. vagina) OR between different organs of the digestive tract
- Bleeding from the stomach, large intestine and/or small intestine (Gastrointestinal bleeding)
- Redness or sores of the palms of the hands or soles of the feet (Palmar-plantar erysdysthesia- "hand-foot syndrome")
- Lack of oxygen to the brain caused by either bleeding in the brain or blood clot. Also called a stroke. (Cerebral vascular accident)
- Leakage of air into the chest cavity surrounding the lung and associated breathing difficulties (Pneumothorax)
- Inflammation of the lungs (Pneumonitis)
- Separation of the retina from its connection at the back of the eye (Retinal tear/retinal detachment)

- Swelling or scarring of the lungs which may cause shortness of breath
- Blood clots in small blood vessels
- Elevated platelets

The company that makes pazopanib has identified a chemical that is present in pazopanib tablets in very small amounts. In laboratory tests, this chemical by itself caused changes to genes (DNA) that indicate that is has the potential to cause cancer or tumors. Exactly what these results mean about your taking pazopanib is not known; however, the risk of harm to you is thought to be low for the following reasons: 1) When pazopanib (which contains a small amount of this impurity) was tested in these same laboratory tests, it did not cause damage to genes; 2) Many cancer drugs have the potential to damage genes, but the benefits of these drugs are believed to be greater than their risks in patients with cancer.

As with any medication, allergic reactions are a possibility.

The risks of drawing blood for a study sample include pain, bruising, or rarely, infection at the site of the needle stick.

You will be exposed to radiation in this research study. The amount of radiation you will receive has a low risk of harmful effects.

There may also be a risk of death.

Your doctor will discuss the risks of tests and procedures that are part of your standard clinical care.

Pregnancy and Birth Control:

1) Will women of child-bearing-potential be allowed to participate in this study?

   Yes: Women of child-bearing-potential will be able to participate in this study if they have a negative pregnancy test and agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

2) Will pregnant and/or nursing women be allowed to participate in this study?

   No: There is not enough medical information to know what the risks might be to an unborn child carried by a woman who takes part in this study.

3) Do you need to have a pregnancy test done to be part of the study?

   Yes: As part of this study a pregnancy test is required for all women who are able to become pregnant.

   A blood pregnancy test will be done by taking blood from your arm.

   You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

4) Will men who are able to father a child be allowed to participate in this study?

   Yes: Men who are able to father a child will be able to participate in this study if they agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

5) What types of birth control are acceptable (for 21 days after last dose of investigational product)?

   Surgical sterilization
   Approved hormonal contraceptives (such as birth control pills, Depo-Provera)
   Barrier methods (such as a condom or diaphragm) used with a spermicide
   An intrauterine device (IUD)
   Complete abstinence for 14 days prior to investigational product

7. Are there reasons you might leave this research study early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers, Novartis, or Mayo may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- if the study is stopped.

We will tell you about any new information that may affect your willingness to stay in the research study.

8. What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment, and follow-up care as needed.

Who will pay for the treatment of research related injuries:

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

Signing this consent form does not change any legal rights you may have.

9. What are the possible benefits from being in this research study?

This study may not make your health better. However, if your cancer responds to the study drug, it may slow the growth of your cancer.

10. What alternative do you have if you choose not to participate in this research study?

You do not have to be in this study to receive treatment for your condition. Your other choices may include:

- Chemotherapy
- Targeted therapy
- Another research study
- You may also choose not to have any treatment except medications to make you feel better.

You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.

11. What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Thyroid function test at screening
- Echocardiogram at screening
- Mandatory tumor tissue biopsy
- Electrocardiogram at screening

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care. These tests and procedures are:

- Standard of care physical examinations
- Standard of care blood and urine tests
- Standard of care thyroid tests after screening
- Standard of care CT/MRI scans
- Bone scan (if applicable)
- Pregnancy test (if applicable)
- Standard of care electrocardiograms after screening
- Standard of care echocardiograms after screening

If you have billing or insurance questions, call Research Billing at the telephone number provided in the Contact Information section of this form.

Novartis (the study sponsor), is providing the study drug free of charge to all patients.

If you have billing or insurance questions call Research Billing at the telephone number provided in the Contact Information section of this form.

12. Will you be paid for taking part in this research study?

You will not be paid for taking part in this study.

13. What will happen to your samples?

We would like to keep your sample for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

1. I permit my sample to be stored and used in future research of renal cancer at Mayo Clinic:

   ☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

   ☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my sample to researchers at other institutions:

   ☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the Contact Information section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

14. How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. The confidentiality of subjects' data will be safeguarded by coding data or samples with numbers, storing research materials in locked cabinets, and password-protecting data stored on a computer.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission.

Health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

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

- To do the research.
- To report the results.
- To see if the research was done correctly.

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

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.
- Novartis.

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- Novartis, and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study.

If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Subject Advocate at: researchsubjectadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission lasts forever, unless you cancel it.

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Name and Clinic Number

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ENROLLMENT AND PERMISSION SIGNATURES

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature