Study Title for Study Participants: Testing combination antibody treatment with trastuzumab and pertuzumab for advanced or metastatic colorectal cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
S1613, "A Randomized Phase II Study of Trastuzumab and Pertuzumab (TP) Compared to Cetuximab and Irinotecan (CETIRI) in Advanced/Metastatic Colorectal Cancer (mCRC) with HER-2 Amplification – Step 2

(S1613 Treatment Consent Form)

What is the usual approach to my colorectal cancer?

You are being asked to take part in this study because you have colorectal cancer which has grown or recurred and has HER2 amplification as tested during the first part of this study. People who are not in a study are usually treated with drugs approved by the FDA, such as 5-fluorounacil, irinotecan, oxaliplatin, bevacizumab, cetuximab, and panitumab. Sometimes, combinations of these are used and your doctor can explain which may be best for you and the extent of benefit with these therapies. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

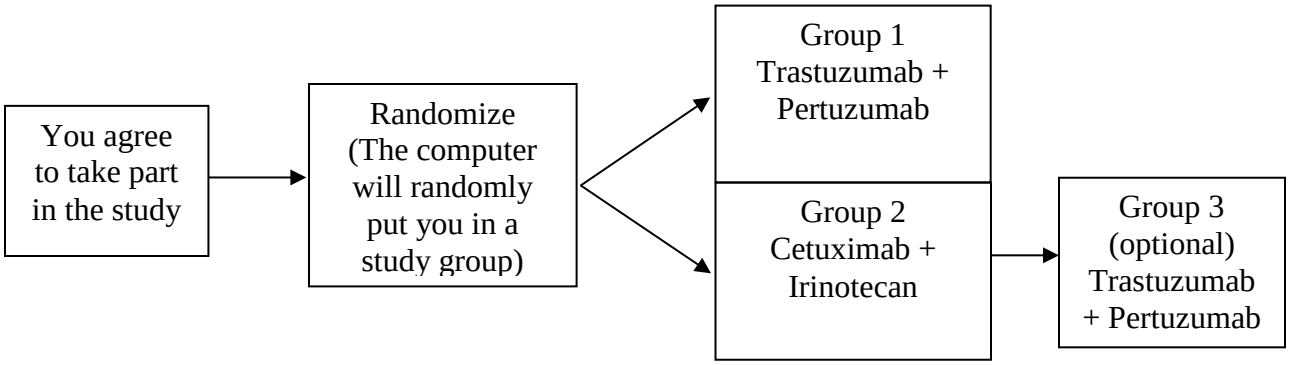
The purpose of this study is to compare any good and bad effects of using a combination of antibodies, trastuzumab and pertuzumab, to using the usual chemotherapy, cetuximab and irinotecan. Treatment with antibodies could shrink your cancer, but it could also cause side effects. This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. The antibody drug combination of trastuzumab and pertuzumab is already FDA-approved for use in HER2 positive breast cancer. There will be about 130 people taking part in this study.

What are the study groups?

This study has three study groups. Group 1 will receive the study drugs trastuzumab and pertuzumab. The combination of trastuzumab and pertuzumab is investigational (not approved by the FDA for treatment of colorectal cancer). These drugs will be given through a vein on Day 1 of every 21 day cycle. Group 2 will receive the usual chemotherapy, cetuximab and irinotecan, through a vein on Day 1 of every 14 day cycle. If you are in Group 2 and your cancer gets worse, you may have the option to receive the same treatment as Group 1, and be placed into Group 3.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

You will receive the study drug until your disease gets worse or until the side effects become too serious to manage. After you finish study treatment, your doctor will continue to watch you for side effects and follow your condition for up to 3 years. If you completed study treatment prior to disease progression (your disease getting worse), then you will be seen by your doctor every 6 weeks and have a physical exam, MRI or CT and lab tests until your disease gets worse and then every 6 months and have a physical exam (and possibly lab tests if your doctor deems necessary) until 3 years after your enrollment to the study. If your disease gets worse prior to being taken off of study treatment, then you will be seen by your doctor every 6 months and have a physical exam (and possibly lab tests if your doctor deems necessary) until 3 years after your enrollment to the study.

What extra tests and procedures will I have if I take part in this study?

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra test. It is not part of the usual approach for your type of cancer.

During the study:

- CT or MRI or PET-CT scan 6 weeks after starting treatment

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that study drugs may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- The study doctor will work with you to treat your side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 - Possible side effects of trastuzumab and pertuzumab

Possible Side Effects of Pertuzumab

COMMON, SOME MAY BE SERIOUS In 100 people receiving pertuzumab, more than 20 and up to 100 may have:
• **Diarrhea, nausea, vomiting** • **Tiredness** • **Infection, especially when white blood cell count is low** • **Hair loss**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pertuzumab, from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Watering eyes** • **Pain** • **Constipation, heartburn** • **Sores in the mouth which may cause difficulty swallowing** • **Swelling of the body** • **Fever** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Swelling and redness of the area of radiation** • **Loss of appetite** • **Dizziness, headache** • **Changes in taste** • **Feeling of "pins and needles" in arms and legs** • **Muscle weakness** • **Numbness, tingling or pain of the arms and legs** • **Difficulty sleeping** • **Cough, shortness of breath** • **Nose bleed** • **Dry skin** • **Change in or loss of some or all of the finger or toenails** • **Redness, pain or peeling of palms and soles** • **Itching, rash** • **Hot flashes**

RARE, AND SERIOUS In 100 people receiving pertuzumab, 3 or fewer may have:
• **Heart failure which may cause shortness of breath, swelling of ankles, and tiredness** • **Change in heart function**

Risk Profile for Trastuzumab (Herceptin) (CAEPR Version 2.5, February 7, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving trastuzumab (herceptin), more than 20 and up to 100 may have:
• **Tiredness**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving trastuzumab (herceptin), from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Infection, especially when white blood cell count is low** • **Heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness** • **Fluid in the body** • **Abnormal heartbeat** • **Watering eyes** • **Pain** • **Diarrhea, nausea, vomiting** • **Sores in the mouth which may cause difficulty swallowing** • **Chills, fever** • **Swelling of the body** • **Flu-like symptoms including body aches** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Change in heart function** • **Weight loss, loss of appetite** • **Changes in taste** • **Headache** • **Numbness, tingling or pain of the arms and legs** • **Depression** • **Difficulty sleeping** • **Stuffy nose** • **Cough, shortness of breath** • **Hair loss, acne, rash, hives** • **Loss of some or all of the nails** • **Hot flashes** • **High blood pressure which may cause headaches, dizziness, blurred vision** • **Low blood pressure which may cause feeling faint**

RARE, AND SERIOUS In 100 people receiving trastuzumab (herceptin), 3 or fewer may have:
• **Damage to organs (lungs, others) which may cause shortness of breath** • **Scarring of the lungs**

Study Group 2 - Possible side effects of cetuximab and irinotecan, which is the usual approach for this type of cancer:

Possible Side Effects of Cetuximab

COMMON, SOME MAY BE SERIOUS **In 100 people receiving Cetuximab, more than 20 and up to 100 may have:**
• **Change in nails** • **Swelling and redness of the area of radiation** • **Rash, itching, dry skin, acne** • **Diarrhea, constipation, nausea, vomiting, loss of appetite, weight loss** • **Sores in mouth which may cause difficulty swallowing** • **Infection, especially when white blood cell count is low** • **Difficulty sleeping** • **Headache, tiredness** • **Numbness and tingling of the arms and legs** • **Blurred vision** • **Shortness of breath, cough** • **Fever** • **Pain**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving Cetuximab, from 4 to 20 may have:**
• **Hair loss** • **Severe skin rash with blisters and can involve inside of mouth and other parts of the body** • **Blood clot which may cause swelling, pain, shortness of breath** • **Allergic reaction or infusion reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat**

RARE, AND SERIOUS **In 100 people receiving Cetuximab, 3 or fewer may have:**
• **Heart stops beating** • **Kidney damage which may require dialysis** • **Scarring of the lungs** • **Severe blood Infection** • **Sudden death**

Possible Side Effects of Irinotecan

COMMON, SOME MAY BE SERIOUS **In 100 people receiving Irinotecan, more than 20 and up to 100 may have:**
• **Severe diarrhea** • **Constipation, nausea, vomiting** • **Weakness** • **Infection, especially when white blood cell count is low** • **Hair loss** • **Loss of appetite, weight loss** • **Anemia which may cause tiredness, or may require a blood transfusion** • **Fever, pain** • **Dizziness, tiredness** • **Cough, shortness of breath** • **Sores in mouth** • **Rash** • **Bruising, bleeding**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving Irinotecan, from 4 to 20 may have:**
• **A tear or hole in internal organs that may require surgery** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Damage to the heart** • **Blood clot which may cause swelling, pain, shortness of breath** • **Scarring of the lungs**

RARE, AND SERIOUS **In 100 people receiving Irinotecan, 3 or fewer may have:**
• **None**

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study and for at least 7 months after stopping study treatment.

Cetuximab causes sensitivity to sunlight, so you should avoid long periods in the sun. You should wear long sleeve shirts, pants, hat, and use sun block protection (SPF 30 or higher) when you are in the sun. Exposing your skin to sunlight while on study could cause severe damage to it.

While on the study, use caution when using over-the-counter products, herbal medicines, or prescribed drugs. You should check with your study team before taking any of those drugs. St. John Wort and ketoconazole are not allowed during irinotecan treatment. Irinotecan is associated with multiple drug interactions. Drug interactions may result in severe side effects. To reduce the chance of drug interactions, please tell your study doctor and his/her staff about any medications (prescription, over-the counter, and vitamin) you are taking during the study.

Imaging Risks
The CT or MRI that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT or MRI that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as 3 years of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

As part of the CT or MRI that you get in this study, iodine will be injected into your vein. Some people are allergic to iodine. Let your study doctor know if you have an allergy to iodine or seafood or if you have kidney problems.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study drugs are better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

What are the costs of taking part in this study?

For those in Group 1 and 3, the trastuzumab and pertuzumab will be supplied at no charge while you take part in this study. The cost of getting the trastuzumab and pertuzumab ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that the trastuzumab and pertuzumab may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

For those in Group 2, the cetuximab and irinotecan will not be supplied by the study and you and/or your health plan/insurance company will need to pay for this treatment.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

The Week 6 CT or MRI will be paid for by the study for all patients. The remaining scans are standard of care that will not be paid for by the study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent

cover page. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor, SWOG, and any drug company supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.
- Alliance
- ECOG-ACRIN
- NRG

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following study.

1. Optional Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part, tissue and blood will be collected and stored in a biobank. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by *SWOG* and supported by the National Cancer Institute.

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) A sample of tissue that has already been collected by your doctor *(archived tissue),* will be collected.
2) Samples of blood will be collected throughout the study.

3) Your sample and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
4) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
6) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and SWOG staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom *SWOG* sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?
You will not benefit from taking part.

ARE THERE ANY COSTS OR PAYMENTS?
There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?
If you decide you no longer want your samples to be used, you can call the study doctor, who will let the researchers know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?
If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES **NO**

This is the end of the section about optional studies.

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)