NCI Community Oncology Research Program – Kansas City (NCORP-KC)

Consent Form

Study Title for Study Participants: Testing the Addition of Ruxolitinib to the Usual Treatment (Tyrosine Kinase Inhibitors) for Chronic Myeloid Leukemia

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
S1712, A Randomized Phase II Study of Ruxolitinib (NSC-752295) in Combination with BCR-ABL Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia (CML) Patients with Molecular Evidence of Disease

What is the usual approach to my CML?

You are being asked to take part in this study because you have chronic myeloid leukemia (CML) with BCR-ABL in your blood. BCR-ABL is a protein that your body makes because of your CML. People who are not in a study are usually treated with drugs called tyrosine kinase inhibitors (TKIs). These drugs are approved by the FDA to treat CML. For patients who receive the usual approach for this cancer, more than half (> 50%) still have disease that can be measured in the blood after five years of treatment.

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 the good and bad effects of adding the study drug ruxolitinib to the usual chemotherapy (called TKI) with the good and bad effects of using TKI alone.

CML cells produce a protein called BCR-ABL. The BCR-ABL protein helps CML cells to grow and divide. The TKI stops the BCR-ABL protein from working, which helps to reduce the amount of CML cells in the body. This is the standard treatment for CML.

Ruxolitinib is a different type of drug that helps to stop the body from making substances called growth factors. CML cells need growth factors to grow and divide. The addition of ruxolitinib to the TKI may or may not help reduce the amount of CML cells in your body, but it could also cause side effects. This study will allow the researchers to look at whether this different approach is better, the same, or worse than the usual approach.

To be better, adding the study drug to TKI treatment should reduce the amount of disease in the blood enough so that it cannot be measured. The study doctors cannot guarantee that you will be helped by adding ruxolitinib to your TKI, but, if you are, the amount of CML cells in your body may decrease.

The TKI drugs on this study are dasatinib and nilotinib. Both of those drugs are FDA approved to treat CML. You will stay on whichever TKI you are already taking. The study drug ruxolitinib is FDA-approved for use in myelofibrosis, but it is not approved to treat CML.

There will be about 84 people taking part in this study.

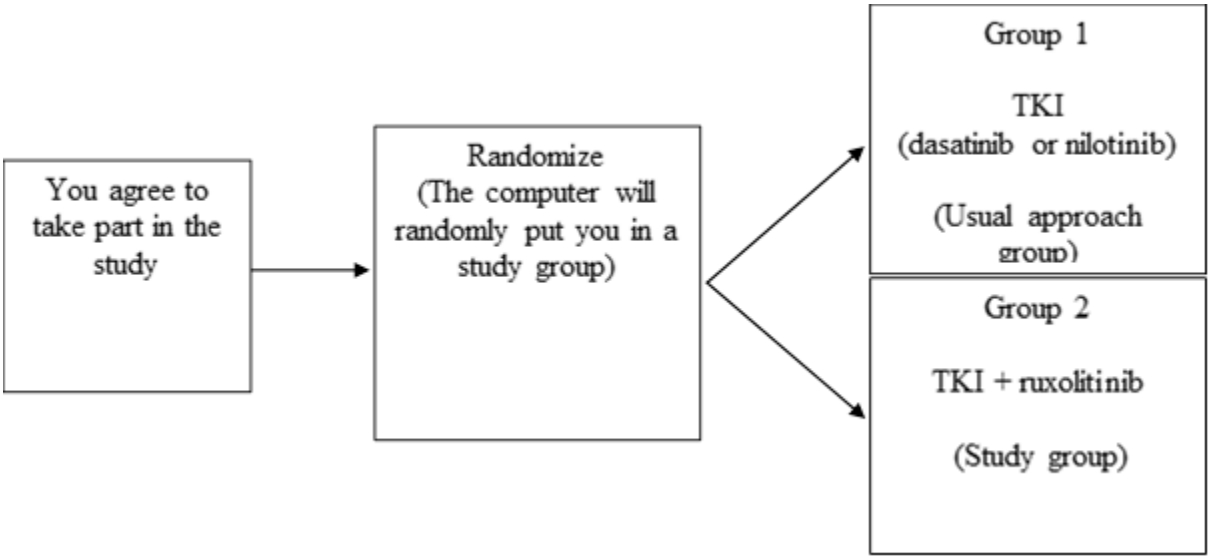
What are the study groups?

This study has two study groups. Group 1 will continue to receive the TKI (either dasatinib or nilotinib) that they are already receiving to treat their CML. Group 2 will receive the TKI (either dasatinib or nilotinib) that they are already receiving to treat their CML, and will also receive the study drug ruxolitinib twice a day.

In both groups, patients will receive their assigned drugs in "cycles" that last 90 days each. There is no break between cycles. Patients will get up to 4 cycles of treatment.

A computer will assign you to one of the treatment groups in the study by chance. 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 treatment on the study for about one year. After you finish the study treatment, your doctor will continue to watch you for side effects and follow your condition for five years after the time you start the study. The treatment and follow up visits will be out-patient. This mean you will not be admitted to the hospital, unless your doctor feels it is necessary. After you finish the study, you may continue to take the TKI that you took during the study, or you and your doctor may decide to change your treatment.

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

All of the exams, tests, and procedures you will have are part of the usual approach for your cancer.

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:

- **You may lose time at work or home and spend more time in the hospital or doctor's office than usual**
- **You may be asked sensitive or private questions which you normally do not discuss**
- **The study drug/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.**

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 be testing 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 drug(s)/study approach.

Here are important points 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 interfere with your ability to have children.**
- **Some side effects may be serious and may even result in death.**

Here are important points about how you and the study doctor can make side effects less of a problem:

- **Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.**
- **The study doctor may be able to treat some 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 that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss them with you.

Also, because of how the drug works, you should avoid eating grapefruit or drinking grapefruit juice while taking dasatinib or nilotinib. You should also avoid taking antacids while taking dasatinib. If antacids must be used, take them either 2 hours before or 2 hours after taking your dose of dasatinib.

<u>TKIs - Study Group 1 and Group 2</u>-

Patients in both study groups will keep taking the TKI that they are already taking (either dasatinib or nilotinib). The risks of these drugs are in the tables below. The risks are the same as they have been the whole time you have been taking the TKI. Being on the study does not change the risks of the TKI.

Possible side effects of dasatinib

COMMON, SOME MAY BE SERIOUS **In 100 people receiving dasatinib, more than 20 and up to 100 may have:**
• **Anemia which may require blood transfusion** • **Diarrhea, nausea** • **Tiredness** • **Bruising, bleeding** • **Pain** • **Headache** • **Shortness of breath** • **Fluid in the body** • **Rash**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving dasatinib, from 4 to 20 may have:**
• **Infection, especially when white blood cell count is low** • **Bloating, constipation, heartburn, vomiting** • **Bleeding from multiple sites** • **Internal bleeding which may cause black tarry stool or blood in vomit** • **Sores in mouth which may cause difficulty swallowing** • **Swelling of the body which may cause shortness of breath** • **Fever** • **Weight gain** • **Weight loss, loss of appetite** • **Dizziness** • **Cough, sore throat** • **Hair loss, itching, acne** • **Flushing**

RARE, AND SERIOUS In 100 people receiving dasatinib, 3 or fewer may have:
• **Heart failure or heart attack which may cause shortness of breath, swelling of ankles, and tiredness** • **Change in the heart rhythm** • **Kidney damage which may require dialysis** • **Bleeding in the brain which may cause confusion** • **Severe skin rash with blisters and peeling which can involve the mouth and other parts of the body** • **Damage to organs which may cause changes in thinking** • **Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)**

Reproductive Risk: Because the effects of the study drugs on sperm are not known, you should not father a child while you are on the study or for 3 months after stopping dasatinib. Women should not be pregnant or nursing, and should not become pregnant for at least 30 days after stopping study drug, because of the possibility that the study drugs might cause harm to the baby. Your study doctor will talk to you about effective methods of pregnancy prevention.

Possible side effects of nilotinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving nilotinib, more than 20 and up to 100 may have:
• **Rash, Itching** • **Nausea** • **Constipation** • **Headache** • **Tiredness** • **Pain in joints** • **Flu-like symptoms including fever, chills, body aches, muscle pain** • **Bruising, bleeding** • **Infection, especially when white blood cell count is low**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving nilotinib, from 4 to 20 may have:**
• **Dizziness** • **Difficulty sleeping** • **Hair loss** • **Pain in muscles** • **Pain in belly** • **Indigestion** • **Diarrhea** • **Dry skin** • **Muscle spasms** • **Pain in arms or legs** • **Pain in back** • **Cough** • **Pain in mouth or throat** • **Shortness of breath** • **Swelling of arms or legs** • **Vomiting** • **Nose bleed** • **Infection** • **Influenza** • **High blood pressure** • **Anemia which may cause tiredness, or may require blood transfusions**

RARE, AND SERIOUS **In 100 people receiving nilotinib, 3 or fewer may have:**
• **Change in the heart rhythm** • **Blockage of an artery (blood vessel), usually with a blood clot** • **Sudden deaths**

Reproductive Risk: Because the effects of the study drugs on sperm are not known, you should not father a child while you are on the study. Women should not be pregnant or nursing because of the possibility that the study drugs might cause harm to the baby. Your study doctor will talk to you about effective methods of pregnancy prevention.

Study Group 2-

Possible side effects of ruxolitinib

COMMON, SOME MAY BE SERIOUS **In 100 people receiving ruxolitinib, more than 20 and up to 100 may have:**
• **Anemia which may cause tiredness, or may require blood transfusions** • **Bruising, bleeding** • **Diarrhea** • **Tiredness**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving ruxolitinib, from 4 to 20 may have:**
• **Bleeding** • **High blood pressure** • **Constipation** • **Vomiting** • **Cough** • **Increased sweating** • **Difficulty sleeping** • **Infection** • **Loss of appetite** • **Muscle spasm** • **Pain in muscles** • **Pain in arms or legs** • **Pain in back** • **Dizziness** • **Shortness of breath** • **Itching, rash**

RARE, AND SERIOUS **In 100 people receiving ruxolitinib, 3 or fewer may have:**
• **Pain in joints**

Reproductive Risk: Because the effects of the study drugs on sperm are not known, you should not father a child while you are on the study. Women should not be pregnant or nursing because of the possibility that the study drugs might cause harm to the baby. Your study doctor will talk to you about effective methods of pregnancy prevention.

Study Group 1 and Group 2-

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.

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

It is not possible to know at this time if the study drug is 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, Institutional Review Board (IRB, a group of people who review the research with the goal of protecting the people who take part in the study) or the Food and Drug Administration (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, call the Central Institutional Review Board at 888-657-3711.

What are the costs of taking part in this study?

The ruxolitinib will be supplied at no charge while you take part in this study. The cost of getting the ruxolitinib 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 ruxolitinib 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.

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 the TKI, and any 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.

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. 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.

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:

- The study sponsor (SWOG) and any drug company supporting the study (Incyte).
- 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.

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 the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION:

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 studies.

1. Future Contact
I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.
Yes No

2. Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies (please read the following information and answer "yes" or "no" at the end of the section).

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. 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, additional blood will be collected the same time it is being collected as part of your regular cancer care and treatment. There will likely also be blood left over from the blood submission discussed above. 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 Nationwide Children's Hospital and supported by the National Cancer Institute.

WHAT IS INVOLVED?

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

1) About 4 to 8 teaspoons of additional blood will be collected at the same time that blood is being collected as part of your regular cancer care and treatment (while you are being screened for the study, after each of the 4 treatment cycles, and about 6 months after you top the study treatment). The blood will be kept at the biobank. 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.
2) 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
3) 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.
4) 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) The most common risks related to drawing blood are pain and bruising.
2) 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.
3) 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.

4) 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.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

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, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. You can decide whether to have your unused samples destroyed or returned to you. 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, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

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.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. this may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main *study* and any additional studies where I circled "yes."

Participant _____

Participant's signature_____

Date of signature_____

Person obtaining consent_____

Signature of person obtaining consent_____

Date of signature_____

Specimen Consent Supplemental Sheets

How are Specimens Used for Research?

Where do specimens come from?

A specimen may be from a blood sample or from bone marrow, skin, toenails or other body materials. People who are trained to handle specimens and protect donors' rights make sure that the highest standards of quality control are followed by SWOG. Your doctor does not work for SWOG, but has agreed to help collect specimens from many patients. Many doctors across the country are helping in the same way.

Why do people do research with specimens?

Research with specimens can help to find out more about what causes cancer, how to prevent it, how to treat it, and how to cure it. Research using specimens can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

What type of research will be done with my specimen?

Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs. Some research looks at diseases that are passed on in families (called genetic research). Research done with your specimen may look for genetic causes and signs of disease.

How do researchers get the specimen?

Researchers from universities, hospitals, and other health organizations conduct research using specimens. They contact SWOG and request samples for their studies. SWOG reviews the way that these studies will be done, and decides if any of the samples can be used. SWOG gets the specimen and information about you from your hospital, and sends the specimen samples and some information about you to the researcher. SWOG will not send your name, address, phone number, social security number or any other identifying information to the researcher.

Will I find out the results of the research using my specimen?

You will not receive the results of research done with your specimen. This is because research can take a long time and must use specimen samples from many people before results are known. Results from research using your specimen may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

Why do you need information from my health records?

In order to do research with your specimen, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher may include your age, sex, race, diagnosis, treatments and family history. This information is collected by your hospital from your health record and sent to SWOG. If more information is needed, SWOG will send it to the researcher.

Will my name be attached to the records that are given to the researcher?

No. Your name, address, phone number and anything else that could identify you will be removed before they go to the researcher. The researcher will not know who you are.

How could the records be used in ways that might be harmful to me?

If your confidential genetic information is discovered, you may suffer from genetic discrimination. Genetic discrimination occurs if people are treated unfairly because of differences in their genes that increase their chances of getting a certain disease. In the past, this could have resulted in the loss of health insurance or employment. Because of this, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, was passed by Congress to protect Americans from such discrimination. The new law prevents discrimination from health insurers and employers. This act was signed into federal law on May 21, 2008, and went into effect May 2009. This law does not cover life insurance, disability insurance and long-term care insurance.

While this study has safeguards in place to protect your confidential genetic information and to make it extremely unlikely that your identity would be connected with any special studies that are performed on your tissue, it is possible that this information could be discovered by someone who is unauthorized to have access to it.

How am I protected?

SWOG is in charge of making sure that information about you is kept private. SWOG will take careful steps to prevent misuse of records. Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.

What if I have more questions?

If you have any questions, please talk to your doctor or nurse, or call our research review board at 888-657-3711.