ANN & ROBERT H. LURIE CHILDREN'S HOSPITAL OF CHICAGO
INSTITUTIONAL REVIEW BOARD
Adult Consent to Participate in a Research Project
Part 1

Investigators at Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's) and Northwestern University (NU) invite you to consider participating in a research study entitled:

Preventing Life-Threatening Allergic Reactions with Ibrutinib, an FDA-Approved BTK Inhibitor

Sponsored by: The Division of Allergy and Immunology of Northwestern University and carried out by Anne Marie Singh, MD.

This consent form describes a study being done at NU and Lurie Children's. Research studies help us learn more about conditions and possible new treatments. Research studies are voluntary, which means that it is your choice whether to participate in the study. The study staff will also explain the study to you and answer any questions that you may have before you make a decision.

WHY IS THIS STUDY BEING DONE?

Food allergy can be a life-threatening disease, and how often it occurs continues to increase despite public health efforts. Studies have shown that it is less likely that a person will lose their food allergies over time and food allergies can also start in adulthood, so more adults now have life-threatening food allergies. Near fatal and fatal reactions can occur in people with food allergies and can cause serious situations. Even though this disease is common, there are currently no approved therapies for food allergy. The only thing people who have food allergies can do now is to stay away from the things they are allergic to and if an allergic reaction does happen then use an epinephrine pen when the allergic reaction happens. There is a large unmet need for new therapies to prevent serious allergic disease including food allergy and anaphylaxis (rapid and serious onset of an allergic reaction).

Recently, a drug called ibrutinib was approved by the United States Food and Drug Administration (FDA). Although this drug is approved to treat some different forms of cancer, there is a possibility that this drug can also prevent allergic reactions. For this study, ibrutinib is considered an "investigational" drug, meaning this drug has not been approved by the FDA for treatment of allergies. This study is being done to determine if ibrutinib can prevent an allergic reaction, as well as to monitor the safety and effectiveness of the drug.

The study treatment, ibrutinib, is a type of an investigational drug that is called a Bruton's tyrosine kinase (BTK) inhibitor. Ibrutinib works by stopping Bruton's tyrosine kinase, an enzyme (or protein that helps reactions occur) in the body that works during an allergic reaction. By reducing the activity of this enzyme, ibrutinib can help to control the allergic response associated with food allergy. Ibrutinib is in the form of a tablet and is taken by mouth and

swallowed. This is an open-label study, which means that you, the study doctor and the study staff will know that you will receive ibrutinib.

You are being asked to participate in this research study because you have a life-threatening allergy to peanuts and/or tree nuts.

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.

WHAT IS INVOLVED IN THE STUDY AND HOW LONG WILL I BE IN THE STUDY?
This study plans to enroll about 12 participants at Lurie Children's.

As a participant, you will be asked to come to the following study site for the study visits.

- Ann & Robert H. Lurie Children's Hospital in Chicago located at 225 E. Chicago, Chicago, IL 60611; Clinical Research Unit (CRU), 19th Floor

If you choose to be in the study, and you qualify for the study, you will be in the study for at least 4 days and you will have to make at least 3 visits to the study site. The amount of time you are in the study and the number of visits you will have may be more than this depending on how the study treatment works for you. You may have to take 2 to 4 doses of ibrutinib if you are in this study.

At least 3 blood samples will be taken during the course of the study, but this may be more depending on how the study treatment works for you. At least 30 mL of blood (about 2 tablespoons) will be taken at each visit. Extra blood samples may be needed if any of your laboratory tests are not normal or if the study doctor thinks it is necessary for monitoring your health. It is possible that more than one try to take a blood sample may be necessary.

From this point on in these pages, ibrutinib will be called the "study drug" and Ann & Robert H. Lurie Children's Hospital in Chicago located at 225 E. Chicago, 19th Floor, Chicago, IL 60611; Clinical Research Unit (CRU), 19th Floor will be called the "study site". Below is a list of procedures that will take place at each visit while you are in the study.

Schedule of Events

Screening Visit (Visit 1):
To help the study doctor determine if you are eligible to participate in this study, you will be asked to come to the study site for a screening visit. This visit will last approximately 1 hour. The following tests and procedures will be performed:

- You will be asked to read and sign this consent form.
- A complete physical examination will be performed and your vital signs (blood pressure, body temperature, breathing, and pulse rate), and height and weight will be taken.

- A review of your health and medical history, your demographics (such as your gender, race, and other background information), and any medications (prescription, nonprescription, and over-the-counter herbal and dietary) you have taken and are currently taking will be done. The study doctor or study staff will also review with you what medications you are not allowed to take during the study.
- About 2 tablespoons (30 ml) of blood will be taken for laboratory tests (such as complete blood count and kidney and liver function tests).
- You will have an electrocardiogram (ECG), which is a test that records the rhythm of the heart. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.
- If you are female of child-bearing potential, a urine pregnancy test will be done.

Baseline Visit (Visit 2, Day 0):

If you meet the requirements to participate in the study and agree to take part, you will be asked to return to the study site within 7 days or less after the screening visit (Visit 1) for your baseline /Day 0 visit (Visit 2). The baseline visit – Visit 2 -will last approximately 1-2 hours. The following tests and procedures will be performed:

- You will have a skin prick test done. During this test, the study team will put a drop of solution containing the food allergen on your skin. They will use a small plastic probe or needle to gently scratch your skin to let the solution enter the surface. This test is usually not painful and will last about 30 minutes.
- About 2 tablespoons (30 ml) of blood will be taken for laboratory tests (such as complete blood count, kidney and liver function tests, and tests to determine the normal level of substances in your blood that indicate an allergic response).
- If you are female of child-bearing potential, a urine pregnancy test will be done.
- You will be given a supply of study drug to take home. You will take the study drug at the same time every day, swallowed with a glass of water. The study staff will describe in more detail how to take and store the study drug at home.

Study Visits 3, 4 and 5 (Days 2, 4, and 7):

You will be asked to return to the study site for visits on Days 2, 4 and 7 (Visits 3, 4 and 5) following your Baseline Visit (Visit 2). If your blood tests are negative for an allergic response at any of these visits, then you will not take any more study drug and your next visit will be the End of Study Visit.

These visits will last approximately 2 hours. The following tests and procedures will be performed at each visit except for the tests and procedures that have bold print:

- You will have a skin prick test done.
- About 2 tablespoons (30 ml) of blood will be taken for laboratory tests (such as complete blood count, kidney and liver function tests, and tests for an allergic response).
- If you are female of child-bearing potential, a urine pregnancy test will be done **(Visit 4 or 5 only)**.

- You may be given a supply of study drug to take home, depending on test results for an allergic response. You will take the study drug at the same time every day, swallowed with a glass of water. The study staff will describe in more detail how to take and store the study drug at home **(Visits 3 and 4 only)**.

Preliminary results have shown that allergy testing is negative by Day 7. Once allergy testing is negative, no further medication is given, and your participation in the study will be finished and you will not have any further study procedures.

Weekly Follow-Up Visits/Early Termination Visit:
Preliminary results have shown that allergy testing is negative by Day 7. If your allergy testing is not negative by Day 7 (Visit 5), you will be asked to return to the study site once a week for safety follow-up visit(s). You will be asked to attend as many visits as needed until allergic response testing returns to baseline (levels before to drug treatment). Once your blood tests are negative for an allergic response at any of these visits, then your next visit will be the End of Study Visit. If you and/or the study doctor decide that you will no longer be in the study before your last visit, you will be asked to complete an Early Termination Visit, which will have the same procedures as listed below.

These visits will last approximately 2 hours. The following tests and procedures will be performed:

- You will have a skin prick test done.
- About 2 tablespoons (30 ml) of blood will be taken for laboratory tests (such as complete blood count, kidney and liver function tests, and tests for an allergic response).
- If you are female of child-bearing potential, a urine pregnancy test will be done.

End of Study Visit:
This will be your last visit for the study. This visit will last approximately 1 hour. The following tests and procedures will be performed:

- A review of any illness or medical events you've had and any medications (prescription and over-the-counter) that have changed since your last visit.
- A complete physical examination will be performed and your vital signs (blood pressure, bod temperature, breathing, and pulse rate), and height and weight will be taken.
- About 2 tablespoons (30 ml) of blood will be taken for laboratory tests (such as kidney and liver function tests and tests for an allergic response).
- You will have an electrocardiogram (ECG).
- If you are female of child-bearing potential, a urine pregnancy test will be done.

ARE THERE BENEFITS (GOOD THINGS) TO TAKING PART IN THE STUDY?
You may or may not have any direct benefit from being in this research study. Your condition may or may not improve or may worsen while participating in the study. The information from this study might help to develop better treatments in the future for people with food allergies.

WHAT ARE THE POSSIBLE RISKS OR SIDE EFFECTS (BAD THINGS) OF THE STUDY?
You might have some side effects and discomfort while participating in this research.

Ibrutinib:
All drugs may cause certain side effects and discomforts.
The most common and expected side effects and discomforts reported for ibrutinib are:

- Diarrhea
- Nausea/vomiting
- Constipation
- Decreased appetite
- Fatigue
- Insomnia (trouble sleeping)
- Headache
- Muscle spasms
- Other pain
- Fever
- Rash
- Cough
- Shortness of breath
- Joint pain
- Edema (swelling)

Additional side effects have been seen in some participants given ibrutinib:

- Hemorrhage (bleeding)
- Infections
- Bone marrow suppression
- Renal (kidney) failure

To date, only people with cancer have received ibrutinib. The cancers being treated with this drug tend to be cancers of older adults, and most of the study subjects have been over the age of 50, with many aged 65 or older. All have received drug for months to years. Most have received ibrutinib after failing other treatments, or in addition to other treatments for their underlying cancer. In this study, you will receive a minimum of 2 daily doses and a maximum of 7 daily doses.

Other types of cancers (range, 5 to 16%) have occurred in patients treated with ibrutinib. The most frequent was non-melanoma (starting at the skin's surface, usually caused by too much sun exposure over many years) skin cancer (range, 4 to 13%). In most studies, the frequency of these cancers was higher in those who received ibrutinib compared to those who did not, but in one study, the frequency of other cancers (particularly non-melanoma skin cancer) was similar in those who received ibrutinib versus those who did not, 24 (8%) vs 23 (8%), respectively. The risk of cancer from taking 2-7 days of this drug in people without cancer is not known.

If you have any problems, you should tell the study doctor or staff as soon as possible. They will watch you closely. If it is best for you, the study doctor may decide to take you out of the study. If you are taken out of the study, the study doctor may want to continue checking on you.

The study drug may have side effects that are unknown today and may include your food allergies getting worse. This is why it is very important for you to report any reactions or changes in your health to the study doctor.

The study staff will monitor any side effects you have during the study. If necessary, you will be withdrawn from the study for your safety.

Allergic Reactions:

As with any drug, there is a risk of an allergic reaction to the study drug ingredients. It is important to tell the study doctor if you are having an allergic reaction.
If you have a very serious allergic reaction, you may be at risk of death. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- A rash (red or rough skin)
- Having a hard time breathing
- Wheezing when breathing
- Sudden drop in blood pressure (making you feel dizzy or lightheaded)
- Not able to breathe without help
- A feeling of dread
- Swelling around the mouth, throat, eyes or other parts of the body
- Fast pulse
- Sweating

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

In the event of an emergency, dial 911 immediately. If you require emergency care, be sure to tell the emergency care provider about your participation in this study.

Study Procedure Risks:

Blood Draws:

When a sample of your blood is taken, you may have some temporary discomfort, pain, bruising, swelling and/or, in rare circumstances, infection at the needle site. Lightheadedness (feeling dizzy) and/or fainting may also occur during or shortly after the blood draw.
The study staff may offer to use numbing cream (containing lidocaine, a topical anesthetic) at the site of your blood draw, and the study doctor can discuss with you any possible side effects of this cream. To minimize these risks, only trained professionals will take your blood.

Electrocardiogram (ECG):
The sticky pads used for this test may cause skin irritation. Taking the sticky pads off causes discomfort similar to when taking off a band-aid.

Unknown/Unforeseeable Risks:
In addition to the risks listed above, there may be some unknown or not common and not yet known risks associated with the use of this study drug, including interaction with other medication you may be taking. For that reason, it is very important that you tell the study doctor about all medications or supplements you are taking during the study.

There is a risk of loss of confidentiality and/or privacy of your information. You will read more about the protection of your information later in this form. Please ask the study doctor if you would like to know more about how your information will be protected while you are participating in this study.

ARE THERE RISKS IF I BECOME PREGNANT DURING THE STUDY?
You should not participate in this study if you are pregnant, planning to become pregnant during the study, or are breastfeeding. The possible side effects to an unborn or breastfed child are not known at this time. Some drugs cause females to have their babies prematurely (early) or to have babies with birth defects.

If you are sexually active, you must agree to use a medically acceptable method of birth control. The study doctor will talk to you about birth control methods you must use during the study.

If you become pregnant while participating in the study, you must notify the study doctor or study staff immediately. If you become pregnant, you will have to withdraw from the study. The study doctor may ask for information about your pregnancy and the birth of the baby.
The study doctor or study staff may share this information with the sponsor.

All participants (both men and women) must agree to use one of the acceptable methods of birth control throughout the study from the Screening Visit until 90 days after stopping study drug.

Birth Control:
Birth control methods considered acceptable for this study include:

- Abstinence
- Oral contraceptives
- Transdermal, intrauterine, injected, or implanted hormonal methods of contraception
- Condom with spermicidal foam/gel/film/cream/suppository
- Male partner with a vasectomy for at least 4 months
- Tubal ligation
- Surgically sterile such as hysterectomy

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this research study. Instead of being in this research study, you can follow standard of care treatments which include avoiding the allergen and the use of self-injected epinephrine after an allergic reaction has occurred.

WHAT IF MY DOCTOR OR I DO NOT THINK I SHOULD STAY ON THE STUDY?
Your participation in this study is voluntary, and you may end participation in this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you decide to end your participation, you will be asked to come into the office for an early termination visit. Information from this visit may be used to check on your health or for research. All the procedures listed under the End of Study/Early Termination Visit will be performed for the visit.

The study doctor may stop your participation in this study at any time (even if you want to stay in the study) if he or she decides that it is in your best interest, if you do not follow study instructions, or if you have a severe side effect. In addition, you may be removed from the study if the study is cancelled by the FDA and/or the Institutional Review Board (IRB).

WHAT ARE THE COSTS?
Neither you nor your insurance company is responsible for costs associated with any tests, procedures and/or medications done for research purposes only. However, you and/or your insurance company are still responsible for the usual, ongoing medical care that is necessary to treat your medical condition.

Since all tests and procedures are performed in this study are for research, there will be no costs to you for being this study.

WILL I BE TOLD ABOUT NEW INFORMATION?
We will tell you if we learn new information that may make you change your mind about being in this study.

WILL I BE COMPENSATED FOR MY PARTICIPATION?
You will receive $50 per each completed study visit for your time and effort and to reimburse you for traveling and parking costs, meals, and possible lost wages. You will be paid in the form of cash at the end of each study visit.

If you do not complete the study, you will only be paid for the visits you complete.

Due to the possible total amount of payment from this study, you will need to fill out an Internal Revenue Service (IRS) W-9 tax form. On this form, the Accounts Payable Office of Lurie Children's or NU/NMH may collect your name, address, and social security number or individual taxpayer identification number (ITIN). This information is required so that the Accounts Payable Office can process your study payment check(s) and for income reporting purposes for which Lurie Children's and/or NU/NMH are obligated by federal law to report. This is because under current federal tax law, the Accounts Payable Office is required to report

payment(s) to the IRS, for anyone paid more than $600 in a calendar year. This information on the W-9 tax form will not be maintained in the study records.

WHAT DO I DO IF I AM INJURED?
If you are injured, medical facilities and treatment will be available. However, you may be required to pay a reasonable fee for such care. You can still receive medical benefits if otherwise entitled. If you have any questions or desire further information concerning the availability of medical care, you may contact Dr. Michael Kelleher, Chief Medical Officer, Lurie Children's, 225 East Chicago Avenue, Box #2, Chicago, Illinois, 60611 (312) 227-4270.

WHO WILL KNOW ABOUT WHAT I DID IN THE STUDY OR HAVE ACCESS TO MY PRIVATE INFORMATION?
This signed consent form will be placed in your medical record at Lurie Children's with a copy placed in the Principal Investigator's research file. Some or all of the research results may be included in your medical records. If you do not have a medical record at Lurie Children's, then this signed consent form will only be kept in the Principal Investigator's research file.

The purpose of clinical studies is to collect medical information from a group of participants to see how well the drug or treatment actually works. Therefore, the investigators/researchers need access to the medical records of the persons who participate in this study**.**

The following information will be collected about you as a part of this research includes:

- Routine medical history, physical exam and blood and urine tests
- Results of the blood and urine tests, questionnaires, and any other procedures performed during the study
- Medical records related to your medical history and treatment

If you sign this consent form, you give permission for your study doctor and Lurie Children's to provide your medical records, personal health information, and the results of the study to the following people, agencies or companies to review and use in this research study:

- Lurie Children's study staff
- Lurie Children's Institutional Review Board (the committee that is in charge of protecting the rights of all adults and children who participate in research studies at Lurie Children's)
- Representatives of Northwestern University
- Northwestern University's study staff
- Northwestern University's Institutional Review Board
- Representatives of the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) or other regulatory agencies

Lurie Children's and your doctors will keep the records of this study confidential, and will release your medical information only to the people, organizations, or companies listed above.

However, you should understand that, once your doctor or Lurie Children's releases your medical information outside of Lurie Children's to these people, organizations, or companies, your doctor or Lurie Children's cannot guarantee that your information will remain confidential. It is possible that these other persons or companies could give your study information to others, without your permission.

You will not be identified individually in any written or oral reports of this study to professionals or the media.

WHAT ARE MY RIGHTS AS A PARTICIPANT?
By signing this consent form, you agree to take part in this study. You are not giving up any of your legal rights or releasing this hospital from responsibility for carelessness.

You may cancel your consent and take yourself out of this study at any time. You will not be penalized for doing this. Your treatment by, and relations with the physician(s) and staff at Lurie Children's, now and in the future, will not be affected in any way if you do not want to take part in this study, or if you enter into the study and then withdraw from it.

At any time, you can tell your study doctor or Lurie Children's not to use or give out your study information or other information from your medical record to other people, organizations, or companies. Withdrawal of this permission must be in writing. Any study information or other information from your medical record collected before your written notice of permission withdrawal may still be used for the study, if that information is necessary for the study. Because the purpose of this study is to collect information about how well the study drug or treatment works, if you refuse to release your study information, you may not be able to start, or continue taking part in this study. Your decision will not affect your regular care and your doctor will not change his or her feelings about you.

If you agree to take part in this research study, you will not be able to look at or ask for a copy of your health information collected only for this study, while you are taking part in the study. If you wish, you will be able to ask for this study research information when the study is over or when you are no longer taking part in the study. This does not affect your right to see your medical record or the results of tests related to regular medical care that is given during the same time as the research study.

If you have any questions about the research methods, you should contact the study doctor, Bruce Bochner, MD, at (312) 503-0068. For questions arising evenings or weekends, you may call Northwestern Memorial Hospital on-call number at 312-649-3154.

If you have any concerns, complaints or general questions about research or your rights as a research participant, and you wish to talk to someone who is not directly involved with this study, contact Catherine Powers, Office of Research Integrity and Compliance, 225 East Chicago Avenue, Box #205, Chicago, IL 60611, (773) 755-7489; cpowers@luriechildrens.org.

You will be given a copy of this consent form.

SIGNATURES

The study has been explained to me and I have read this consent form, have been given the opportunity to consider my decision, and have had all my questions answered. I agree to take part in this study as explained in this consent form. I agree to let my doctor or Lurie Children's and/or NU to use and give out my health information in the way it is described in this consent form until the end of the research study.

Date	Signature of Participant (≥18 years) or Legally Authorized Representative (LAR)
	Printed Name of Research Subject or LAR

I certify that I have explained the above to the subject and believe that the signature(s) was affixed freely. I also agree to answer any questions that may arise.

Date	Signature of Person Obtaining Consent (Investigator or designee)
	Printed Name of Person Obtaining Consent