RUSH

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

Site Principal Investigator: Ruta Rao, MD
Department: Rush University Cancer Center
Address and Contact Information: 1725 W. Harrison Street, Suite 809, Chicago IL 60612
Clinic 24-hr phone: 312-226-2371

Protocol Title: A Phase I Study to Evaluate the Safety of Intratumoral Influenza Vaccine Administration in Patients with Breast Cancer

Funder : Brian Piccolo Cancer Research Fund

Name of Participant: _____

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center ("Rush") will not change or be affected.

The purpose of this study is to see if injecting the seasonal flu vaccine directly into your breast cancer tumor is a safe treatment. We also want to find out if this helps shrink the tumor. Previous studies done at Rush found that this treatment slowed cancer tumor growth in mice. Using the seasonal flu vaccine in this way is considered "investigational," which means it has not been approved by the U.S. Food and Drug Administration (FDA) and it must be tested to see if it is a safe and effective treatment for the disease or condition being studied. The FDA is allowing the use of the seasonal flu vaccine for this research.

If you agree to participate in this study, your participation may last up to 3 months after tumor-removal surgery and you will be asked to complete about 7 clinic visits.

During these visits, you will receive the flu vaccine treatment and a member of the study team will ask about any side effects that you may be experiencing and drugs you are taking. You will have blood and tumor tissue samples taken, and you will have the option to participate in a stool collection sub-study. Data will be collected from your medical records, including lab values and physical exam results. For a detailed list of study procedures, please see the "*What are the activities you will be doing if you participate in this study?*" section of this consent form.

There are risks to you for participating in this study. In this study, there is a risk of redness, swelling, and/or pain at the injection site, stomach upset, and fatigue (feeling tired). For a detailed list of risks you should know about, please see the "*What are the risks and discomforts of participating in this study?*" section of this consent form.

You may benefit from taking part in this study. Based on experience with the seasonal flu vaccine in animals, researchers believe it may be of benefit to people with your condition. However, because individuals respond differently to therapy, no one can know in advance if it will be helpful for you.

You have the option to not participate in this study and to receive standard treatment for your breast cancer.

Detailed Information: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

Why are you being invited to participate in this study?
You are being asked to participate in this study because you have a specific type of breast cancer (HER2+ and TNBC) and you will be receiving neoadjuvant chemotherapy. Neoadjuvant chemotherapy is chemotherapy that a person with cancer receives before their primary course of treatment. The aim is to shrink a cancerous tumor using drugs before moving onto other treatments, such as surgery. Neoadjuvant chemotherapy helps doctors target cancerous growths more easily at a later stage.

If you have had a regular (yearly) flu vaccination injection in your arm, you can still participate in this study. If you have not had a flu vaccine in your arm, you can also still participate in this study.

How many participants will take part in this study?
Up to 18 participants are expected to take part in this study at Rush University Medical Center.

What are the activities you will be doing if you participate in this study?
This study calendar below is a summary of what activities will be done during the study:

	Screening	IT flu shot	IT flu shot	Beginning of Neoadjuvant Chemotherapy Cycle	1 Month Post Surgery	3 Months Post Surgery
Cycle/day	-30 to -8	-6 +/- 1	0 (or 1)	Cycle 1/Day 1 & Cycle 2/Day 1		
Informed Consent	X					
Demographics/Medical History	X					
Physical Examination	X			X	X	X
Height	X					
Vitals signs (including oxygen levels & weight)	X			X	X	X
Prior & current medications	X			X	X	X
Adverse Events	X		X	X	X	X
Biopsy		X	X			
Labs	X	X	X	X		
Stool (optional)	X		X			
Treatment (neoadjuvant chemotherapy)				X		

Screening Period

- Informed consent- you will be asked if you want to participate in this study. If you do, you will sign this informed consent form and a signed copy will be given to you by a member of the study team.
- Demographics/medical history – you will be asked questions about your medical history (procedures or illnesses you have had in the past), current medications you use, and your demographics (race, ethnicity, gender, etc.)
- Physical examination, height, vital signs – a member of the study team will access your medical record to get this information
- Prior medications – you will be asked questions about medications you have used before
- Adverse events – you will be asked about any health issues you are experiencing today
- Labs – you will have blood drawn for study-specific testing (about 20ml or 4 teaspoons)
- Stool collection – this is optional. You will be given a home testing kit and asked to provide a stool sample using a non-invasive swab. Instructions on how to do this will be given to you.

Treatment Period

- You will have two injections of seasonal flu vaccine directly into your breast tumor site (called an "intraturmoral" injection). The doctor will use an ultrasound machine to make sure they inject the vaccine directly into the tumor. An ultrasound machine makes images so that the inside of your body can be seen on a TV or computer monitor. This does not use radiation (like a CAT scan or X-ray).
- Biopsy – on the same days as your flu vaccine injections, the doctor will remove a small piece of your tumor tissue for testing
- Blood samples collected for research purposes
- Adverse events

- Stool collection (optional)

Beginning of Neoadjuvant Chemotherapy Cycles 1 & 2

On Cycle 1 Day 1 and Cycle 2 Day 1, you will be in the clinic for regularly scheduled care and the study team will collect information from your regularly scheduled procedures for this study. These procedures would be done whether or not you were in this study, and include:

- Physical examination & vital signs (accessed from your medical record)
- Prior medications
- Adverse events
- Labs
- You will also receive standard of care treatment (called neoadjuvant chemotherapy)

One Month and Three Months Post-Surgery to Remove the Tumor

- Physical examination & vital signs (accessed from your medical record)
- Prior medications
- Adverse events

Does this study involve tissue/blood banking?

No, it does not. Tissue and/or blood banking is the long-term storage of your samples into a repository (or sample bank).

Does this study involve genetic testing?

Yes, this study involves DNA analysis if participants decide to take part in the optional stool sample collection. The use of genetic material in research to study the causes of disease and to help understand how individuals respond to drug treatments is called genetic research. The cells of your body contain a molecule called deoxyribonucleic acid (DNA). DNA is received from your parents and carries a code in the form of genes, which determine your physical characteristics such as the color of your hair and eyes. Ribonucleic acid or RNA for short also acts as a messenger to tell your cells to produce certain features. Just as differences in our genetic codes help explain why we all look different; these differences can also help explain why some people develop certain diseases and others do not. They may also help explain why some drugs are safe and effective for some people but not for others.

What do you need to know regarding the collection of biospecimens?

Biospecimens may include blood, tissue, urine, bone marrow, saliva, cells, etc. In this study, we will be collecting blood, tumor tissue, and stool samples (optional).

Will your information or biospecimens be used for research in the future?

Information or biospecimens collected from you for this study may be used for future research or shared with other researchers. If this happens, information which could identify you will be removed before any information or biospecimens are shared. Since identifying information will be removed, you will not be asked for additional consent.

Will your cells, tissues, blood or other biological materials (biospecimens) be used to develop commercial products?

No, your biospecimens will not be used to develop a commercial product.

What are the risks and discomforts of participating in this study?

The seasonal flu vaccine is generally well-tolerated, but side effects can occur.

- Greater than 10%
    - Gastrointestinal (stomach issues)
        - Anorexia (loss of appetite) (adults and older adults: 4% to 8%)
        - Diarrhea (4% to 13%)
        - Nausea (feeling sick to your stomach) (≤12%)
        - Vomiting (throwing up) (adults and older adults: ≤3%)
    - Redness at injection site (1% to 37%)
    - Firming or hardening of the skin at injection site (≤17%)
    - Pain at the injection site (17% to 67%)
    - Swelling at the injection site (≤25%)
    - Tenderness at the injection site (21% to 69%)
    - Nervous system
        - Fatigue (tiredness) (≤22%)
        - Headache (1% to 27%)
        - Malaise (generally feeling unwell) (≤38%)
    - Arthralgia (joint pain) (4% to 15%)
    - Myalgia (muscle pain) (8% to 40%)
    - Fever (adults and older adults: ≤4%)

- 1-10%
    - Bruising at injection site (≤9%)
    - Chills (≤7%)
    - Shivering (≤9%)
    - Oropharyngeal (mouth/throat pain) (adolescents and adults: 2% to 7%)

There may be other risks that may happen that we cannot predict.

What are the reproductive risks of participating in this study?

The effects of intratumoral flu vaccine on the developing human fetus are unknown. For this reason, women of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to joining the study and throughout the study period. If a woman becomes pregnant or suspects she is pregnant while she is participating in this study, she should inform her treating doctor immediately. Participants who do not agree to comply with these precautions cannot be in this study.

Pregnant or nursing (breast-feeding) women cannot be in this study because there is an unknown but potential risk to multiple injections of flu vaccine in pregnant or nursing women.

What are the risks involving genetic information?

While we believe that the risks to you and your family are very low, we are not able to know all of the risks from taking part in genetic research. Your privacy will be protected to the fullest extent possible. Certain health concerns that affect you and your blood relatives might be found as inherited traits are studied. Even though your genes are unique, you share some of the same

genes with your blood relatives. Genetic information is considered health information and is protected under the Health Insurance Portability and Accountability Act (HIPAA) as is your other health information. While very rare, information could be misused by employers, insurance companies and others. For example, life insurance companies may charge a higher rate based on this information. A federal law called the Genetic Information Non-Discrimination Act (GINA) should help lower the risk from unfair health insurance or employment policies. To learn more about the GINA Law, please go to http://www.ginahelp.org/GINAhelp.pdf or ask the study staff.

What if there is new information that may affect your decision to participate in this study?
During this study, you will be told about important findings (either good or bad), such as changes in the risks or benefits of participation in the study or new choices to participation that might cause you to change your mind about being in the study. If new information is shared with you, you may be asked to sign a revised consent form in order to continue participating in this study.

Will you receive your individual results from the study?
Generally, activities performed for research purposes are not meant to provide clinical information. We may learn things about you from this study which could be important to your health or treatment. However, we will not share these results with you because these results will not be used clinically to make treatment recommendations and will not affect you care.

Can you leave or be removed from this study?
You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to leave this study. If you leave this study before the final study visit, the study doctor may ask you to complete the final steps.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the instructions;
- The study is cancelled for any reason.

What about confidentiality of your medical information?
This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Ruta Rao, the study team, and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Rao and the study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information

will come from your medical record. The health information that Rush may use or disclose for this research includes: your medical history, physical exam and laboratory test results.

Dr. Rao and the study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers;
- Monitoring agencies such as the Food and Drug Administration (FDA), the National Institutes of Health and the Rush Institutional Review Board (IRB).

While you participate in the study you will have access to your medical record, but Dr. Rao is not required to release to your study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed above.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Ruta Rao at 1725 W. Harrison Street, Suite 809, Chicago IL 60612. If the authorization is revoked, you will no longer be allowed to participate in the study and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

What are the costs to participate in this study?
If you take part in this study, you may have to pay extra costs. Any research-related tests, procedures, or services that you may receive solely for the purposes of this study and which would not be performed otherwise will be provided to you free of charge by Rush. For example, the costs for the required biospy, flu vaccine, flu vaccine administration, optional stool sample collection and testing, and processing of research lab samples will be paid by Rush.

You or your insurance will be responsible for paying for the cost of any routine medical care that you would receive whether you participate in this study or not, unless you are told that such item or service will be supplied at no cost. If you have health insurance, the insurance may or may not pay for the costs associated with your participation in this study. You may have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires. Before you decide to be in this study, you should contact your insurance provider to verify coverage.

Will you be paid for your participation in this study?
You will not be paid for being in this study.

What if you are injured as a result of your participation in this study?
If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. Rao at telephone number 312-226-2371.

You should let any health care provider who treats you know that you are in this study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What other information should you know about?
Investigator Dual-Role
If your doctor is also the person responsible for this study, please note that she is interested in both your clinical care and the conduct of this study. You have the right to discuss this study with another person who is not part of the research team before making your decision whether or not to be in the study.

Who can you contact for more information about this study?
Questions are encouraged. If you have further questions about this study, you may call Dr. Rao at 312-226-2371.

Who can you contact if you have concerns about your rights as a study participant?
Questions about the rights of research participants may be addressed to the Rush University Medical Center Office of Research Affairs at 1-800-876-0772.

What are your rights as a study participant?
Taking part in this study is voluntary. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected.

If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Rao in writing at the address on the first page. Dr. Rao may still use your information that was collected prior to your written notice.

_____(initial) Yes, I would like to participate in the optional stool collection sub-study

_____(initial) No, I do not wish to participate in the optional stool collection sub-study

SIGNATURE BY THE PARTICIPANT:
By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent form. You will be given a signed copy of this consent.

_____	_____	_____
Name of Participant	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the. I further attest that all questions asked by the participant were answered to the best of my knowledge.

_____	_____
Signature of Individual Obtaining Consent	Date of Signature

SIGNATURE BY WITNESS/INTERPRETER:
[*For use if this consent is being used as a written summary of the research along with a short form consent OR when the person obtaining consent is not the witness*]
I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the participant and the person signing the form has done so voluntarily.

_____
Name of Witness/Interpreter

_____	_____
Signature of Witness/Interpreter	Date of Signature