Protocol Title: 5-5-5 Adaptive Bridging Radiation Therapy (ABRT) for Relapsed/Refractory B-cell Lymphoma Prior to CAR T-cell Therapy

DF/HCC Principal Investigator(s) / Institution(s):
Chirayu Patel, MD / Massachusetts General Hospital
Andrea Ng, MD / Dana-Farber Cancer Institute

Main Consent

INTRODUCTION AND KEY INFORMATION

The following is a short summary of this research study to help you decide whether you would like to be a part of this study. More detailed information is provided later in this form.

For purposes of this research, you will be referred to as a "participant."

1. Why am I being invited to take part in a research study?

You are invited to take part in this research study because you have relapsed (your cancer has come back) or refractory (your cancer has not responded to treatment) B-cell Lymphoma and will be undergoing CAR T-cell Therapy.

2. Why is this research being done?

This research is being done to see if a new radiation therapy administration schedule will positively impact the logistics, time, cost, and side effects of radiation therapy.

3. Who is supporting this research?

The Principal Investigator of this study and Massachusetts General Hospital are the primary sponsors of this study.

This study is being funded by Varian, a medical technology company, through a grant.

4. What does this research study involve and how long will it last?

This research study involves radiation therapy.

You will receive radiation therapy every 5 business days (1 week apart) for 5 weeks leading up to your CAR T-cell therapy infusion. You will be followed for 90 days after your CAR T-cell therapy infusion.

5. What are the risks to participating in this study?

There are risks to taking part in any research study. We want to make sure you know about a few common risks right now. There may also be rare, serious and potentially life-threatening side effects. More information about these risks and additional risks are provided in “Section C. What are the risks or discomforts of the research study?”.

There is a risk that you could have side effects from the radiation therapy. These side effects may be worse and may be different than you would get with other approaches for your cancer.

Some of the most common side effects that the study doctors know about are:

- Fatigue
- Nausea
- Temporary worsening of pain

6. Will being in this study benefit me in any way?

We do not know if taking part in this study will benefit you. This study may help researchers learn information that could help people in the future.

7. What are my options?

Instead of being in this research study, you have other options which may include the following:

- Receive standard treatment including a course of daily palliative radiation over 2-3 consecutive weeks (10-15 treatments).
- Decide not to participate in this research study.
- Participate in another research study.
- Receive no therapy specific to your cancer.
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms.

8. Do I have to take part in this research?

All research is voluntary. It is your choice whether you take part in this research or not. If you decide to participate, please sign and date at the end of this form. We will give you a copy and you can refer to this consent form at any time.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions at any time.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Pilot Study, which is the first time investigators are examining this intervention.

In this research study, you will receive radiation therapy once weekly for 5 weeks. This is a novel administration schedule and we're looking to see how this schedule impacts side effects you may experience, the time spent receiving radiation therapy, how much radiation therapy you can receive, and how effective this new schedule is.

It is expected that about 10 people will take part in this research study.

B. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **Medical history,** which includes questions about your health, current medications, and any allergies.
- **Performance status,** which evaluates how you are able to carry on with your usual activities.

If these tests show that you are eligible to participate in the research study, you may begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Additional research procedures to be performed at the time of screening but not required to determine eligibility:

- **Data Collection:** Data will be collected and shared with an outside collaborator for analysis. The data will not be identifiable.

Study Treatment Overview:

- **Radiation Therapy (RT):** You will receive radiation therapy once weekly for up to 5 weeks leading up to your CAR-T cell therapy infusion.

Study Visits: you will have study visits up to 4 weeks prior to Radiation Therapy (RT) administration, weekly for up to 5 weeks during RT administration, 30 days

post-CAR T infusion, and 90 days post-CAR T infusion. These visits will involve the following:

- **Adverse event (AE) assessment,** which includes questions about how you are feeling and whether you are experiencing any side effects.
- **Questionnaires,** you will be asked to complete questionnaires on side effects, financial burden of treatment, and quality of life (satisfaction, happiness). These are expected to take 20 minutes.
- **Scans,** PET-CT (Positron Emission Tomography - Computerized Tomography) or CT-based disease assessment will occur at the 30- and 90-day post-CAR T infusion for disease assessment
- **RT administration** weekly for up to 5 weeks.

Research Study Plan:

	Screening	Within 4 weeks prior to RT start date	RT Administration (5 weeks)	30 Days Post-CAR T	90 Days Post-CAR T
Medical history	X				
Performance status	X				
AE assessment		X	X	X	X
Questionnaires		X	X	X	X
Scans				X	X
RT administration			X		

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal not be removed from the study.

C. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. One risk is that you may get a study intervention that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away. Some may be life-threatening or fatal.

Risks Associated with Radiation Therapy:
In addition to the risks mentioned earlier, other risks will be discussed in this section.

Within 90 Days of Radiation Therapy:

Likely (More than a 5% chance that this will happen)

- Fatigue
- Loss of appetite
- Nausea
- Skin/scalp redness, dryness, itching and/or alopecia (hair loss) within the radiation treatment fields
- Change in taste

Frequent (Between a 1-5% chance that this will happen)

- Imbalance, dizziness, vertigo (spinning sensation)
- Vomiting

Long Term Side Effects

General:

- Second cancers caused by radiation
- Fibrosis (scarring) within the treatment site or adjacent structures

The following late effects are based on site of treatment (listed in **bold**)
Chest:

- Lung inflammation or lung fibrosis - can be seen on imaging, but very rare to cause permanent shortness of breath
- Coronary artery disease/heart disease

GI/Abdomen/Pelvis:

- Difficulty digesting certain foods (uncommon)
- Stomach complications requiring surgery (uncommon)
- Inflammation of the liver (uncommon) which may cause a poor appetite, tiredness, mild fever, muscle or joint aches, feeling sick to

your stomach and vomiting, pain in your belly, yellow eyes and skin, and dark urine
- Liver and/or kidney failure (extremely rare)
- Radiation-induced cancer (extremely rare)
- Infertility or the inability to have children

Bone:
- Permanent loss of hair in the area of treatment
- Mild scarring of skin or muscle without changes in function
- Damage to bone or muscle limiting function, arthritis
- Bone fractures

Brain:
- Sleepiness/Fatigue
- Impaired short-term memory/processing
- Impaired hearing
- Cataracts or clouding of the lens of the eye
- Hormone changes (such as thyroid) which can cause tiredness, constipation, hair loss, sensitivity to heat or cold temperatures, mood changes, sweating, muscle aches, a fast heartbeat or weight changes

Eyes:
- Cataracts or clouding of the lens of the eye
- Dry eye
- Hormone changes which can cause tiredness, constipation, hair loss, sensitivity to heat or cold temperatures, mood changes, sweating, muscle aches, a fast heartbeat or weight changes
- Gradual loss of vision
- Eye pain (rare)
- Injury to nearby brain tissue (rare)

Head and Neck:
- Dry mouth
- Dental problems
- Thickening or darkening of the skin
- Hypothyroidism which can cause tiredness, constipation, hair loss, sensitivity to heat or cold temperatures, mood changes, sweating, muscle aches, a fast heartbeat or weight changes
- Difficulty swallowing
- Severe and/or permanent injury to esophagus causing difficulty swallowing (rare)

- Severe and/or permanent injury to nerves, bones, tissue, or spinal cord causing weakness, numbness (rare)

Spine (Thoracic):

- Lung inflammation causing cough, shortness of breath, and/or fever (rare)
- Lung scarring causing permanent shortness of breath (very rare)
- Severe and/or permanent injury to esophagus, heart, spinal cord, vessels, bones (extremely rare)

Skin:

- Dryness, lightening or darkening of skin
- Hair loss in treatment area
- Fibrosis of subcutaneous (under the skin) tissues
- Necrosis (death of tissue), ulceration (ulcer formation) of skin
- Telangiectasia (new blood vessel formation in treated area)
- Joint stiffness (uncommon)
- Swelling (edema) of treated area (uncommon)
- Radiation-induced cancer (extremely rare)

Reproductive Risks:
The drugs used in this research study may affect a fetus. While participating in this research study, you should not:

- become pregnant
- nurse a baby
- father a biological baby

We can provide counseling about preventing pregnancy for all study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the biological father of a child.

If your partner becomes pregnant while you are on the study, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens.

Non-Physical Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

The questionnaires used in this study may be upsetting. If you find the questionnaires upsetting, you may speak with the research doctor or ask to be referred for additional emotional support. You may also skip any question that you do not wish to answer.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

D. WHAT WILL HAPPEN IF I AM REMOVED FROM THE STUDY OR DECIDE TO END MY PARTICIPATION IN THE RESEARCH?

You may be taken off the research study for any reason including:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- If you have any problems following study treatments and procedures
- You become pregnant or plan to become pregnant
- Your condition worsens
- A decision is made to end the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

You can also choose to stop participating in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. They will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the study.

It is important to note that although you may withdraw from study participation, the FDA requires that any information collected up to the point of your withdrawal not be removed from study records. Additionally, the research doctor may consult public records after you have withdrawn from the study.

E. WHAT ARE THE BENEFITS OF THIS RESEARCH STUDY?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will provide more information about radiation therapy administered in this investigational schedule and relapsed/refractory B-cell lymphoma.

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

G. WHAT ARE YOUR COSTS?

Taking part in this research study may lead to added costs to you or your insurance company. This may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your disease. You may:

- Have more travel costs
- Need to take more time off work
- Have other additional personal costs

You will not be charged for the radiation therapy.

You or your insurance company will be charged for portions of your care during this research study that are considered routine costs. Routine costs ***may*** include services to determine your eligibility, services to prevent (monitor) and diagnose disease, and services to treat side effects. Examples of research study routine costs may include the infusion of the study medicines, office visits, lab tests, procedures, and imaging.

You may be billed for co-payments, co-insurance, premiums and deductibles that are typical for your insurance coverage. Participation may result in additional ***routine costs*** because of more frequent research visits.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Brigham and Women's Hospital: (617) 732-5524 or (617) 732-7485
- Dana-Farber Cancer Institute: (617) 632-3455

- Massachusetts General Hospital: (617) 726-2191

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov
or 1-800-4-CANCER (1-800-422-6237)

H. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research.

These treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans to pay you or give you other compensation for the injury. However, you do not give up any of your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender and sex assigned at birth, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this research. If possible, you should give them a copy of this consent form.

I. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Massachusetts General Hospital

- Chirayu Patel, MD: (617) 724-2430

Dana-Farber Cancer Institute

- Andrea Ng, MD: (617) 394-2668

24-hour contact: Please contact your hospital and ask that your doctor be paged:

- Massachusetts General Hospital at 617-724-4000
- Dana Farber Cancer Institute at 617-632-3000

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

J. RETURN OF RESEARCH RESULTS

Return of Aggregate Results
You may be contacted after the study is completed to ask if you would like to receive a summary of the study results from a publication of aggregate results. You will also be given a chance to opt out of this. You may also be asked to share an email address to receive indication that study results are ready to be shared.

K. CLINICALTRIALS.GOV

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.

L. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study will not be used for any future research after this study is complete.

M. CONFIDENTIALITY

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a research database.

The study team may publish the results of this research study and when we do, we may be asked to make the data we collect available to other researchers. We will not include information that identifies you in any publications.

Information about you and your health is personal and private. Generally, it cannot be obtained without your written permission. By signing this form, you are providing that permission and your information may be obtained and used in accordance with this informed consent and as required or allowed by law. This means that researchers may obtain information regarding your past medical history, as well as specimens and samples from previous health care providers such as hospitals and labs.

N. FINANCIAL DISCLOSURES

It is possible that certain researchers on this study may have earned money from, or own some publicly-traded stock in, the company that makes or is developing the study. The amount of money that a researcher may earn and still take part in research is limited by the Harvard Medical School Faculty of Medicine Policy on Conflicts of Interest and Commitment. If you have further questions, please speak with a member of the study team or contact the Dana-Farber Cancer Institute Office of Research Integrity at 617-432-4557 or researchintegrity@dfci.harvard.edu.

O. GENETIC RESEARCH

This research may involve somatic genetic testing but will not involve germline testing. Somatic testing involves testing or sequencing of your tumor and looks for acquired mutations that may have developed due to your cancer. The results are used to plan treatment, including the use of targeted therapy and immunotherapy.

P. PRIVACY OF PROTECTED HEALTH INFORMATION (HIPAA AUTHORIZATION)

The Health Insurance Portability and Accountability Act (HIPAA) is a federal law that requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition,

other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, representatives, business partners, and its agent(s): DF/HCC
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health

information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

Q. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant _____ Date _____

DFCI Protocol Number: 23-364	Approved Date (DFCI IRB Approval): 08/31/2023
Date Posted for Use: 12/08/2023	

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant or legally authorized representative is a non-English speaker who received and signed the translated Short Form in lieu of English consent document, and was provided a copy

☐ *As someone who understands both English and the language used by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.*

Signature of Interpreter: _____

Signature of Witness: _____
Interpreter may also serve as Witness if present

Printed Name of Interpreter: _____

Printed Name of Witness: _____

Date: _____

☐ 1b) Participant or legally authorized representative is a non-English speaker who received and signed a translated consent form in the language they understand, and was provided a copy

☐ 1c) Participant is unable to sign the consent form because:

- ☐ The participant is unable to read and write.
- ☐ The participant has a physical disability.
- ☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Interpreter: _____

Signature of Witness: _____
Interpreter may also serve as Witness if present

Printed Name of Interpreter: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ 2a) gave permission for the adult participant to participate
- ☐ 2b) did not give permission for the adult participant to participate