Title of Research Study: *A Multi-Center Phase 2 Study of Combined Modality Treatment with Ruxolitinib, Decitabine, and Donor Lymphocyte Infusion for Post-Transplant Relapse of AML or MDS*

Investigator Team Contact Information: *Mark Juckett, MD*
For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Mark Juckett, MD **Investigator Departmental Affiliation:** Division of Hematology, Oncology and Transplantation **Phone Number:** 612-625-8942 **Email Address:** juck0001@umn.edu	**If you need emergency care:** • Call 911 or go to your nearest emergency room right away. **If you do NOT need emergency care:** • Call or go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

The study will be conducted at 3 cancer research centers around the United States; however the University of Minnesota is the lead institution and Dr. Juckett is Principal Investigator for the entire study.

Supported By: This research is supported by Incyte Corporation, who is providing the study drug, Ruxolitinib (also called Jakafi®).

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as

an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

You are being considered for this research because you have AML or MDS that have relapsed after an allogeneic stem cell transplant.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

Patients who have relapsed after a transplant are commonly treated with an infusion of immune cells from their original donor, "Donor Lymphocyte Infusion," (DLI), a second transplant, or chemotherapy with Decitabine or Azacitidine. Although these are all standard treatments, these approaches have had limited success. The problem with DLI or a second transplant is that both treatments use high dose chemotherapy prior to the cell infusion, which increases the risk of graft-versus-host-disease, "GVHD," a condition in which the transplanted cells attack the recipient's body. The problem with Decitabine or Azacitidine chemotherapy alone is that while the cancer responds temporarily to the treatment, it hasn't been shown to bring about long-term remission.

The approach of this research is to pair DLI with Decitabine instead of high dose chemotherapy, then add the research drug, Ruxolitinib. Ruxolitinib is a type of drug called a "JAK inhibitor" and is approved to treat Myelofibrosis (a rare bone marrow cancer). Recent research has shown that JAK inhibitors may help prevent GVHD. The purpose of this study is to see whether combining a standard DLI infusion with chemotherapy and Ruxolitinib will bring about remission with a lesser risk of GVHD.

The study involves an investigational product, Ruxolitinib. Investigational usually means that the drug or device is not approved by the Food and Drug Administration (FDA); however in this case, it means that while Ruxolitinib is approved to treat acute GVHD, it has not been approved as a preventative medication for GVHD. This study is being conducted with the FDA's permission under an Investigational New Drug (IND) application.

How long will the research last?

We expect that you will be in this research study for up to 25 months - up to 13 months of active treatment and 12 months of follow up. You may receive up to 4 cycles of treatment. Depending on how many times you receive the treatment, you may have up to 21 assessments in the clinic or in the inpatient unit. These assessments will generally take about an hour.

What will I need to do to participate?

You will be asked:

- to undergo the DLI and Decitabine for up to four cycles,
- take the Ruxolitinib twice a day from the beginning of cycle one until six months after you complete the last cycle,
- come to the clinic, or be assessed in the inpatient unit, for up to 21 study visits,
- provide blood samples (about 3.5 tablespoons) up to 9 times, and
- provide a bone marrow sample 3 times.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

While DLI and Decitabine are standard treatments for post transplantation relapse, combining them, and adding Ruxolitinib is considered research. While we believe that this approach will be less toxic than DLI and high dose chemotherapy, and more likely to achieve remission than decitabine alone, there is no guarantee that it will be less toxic and more effective than standard treatments alone.

The most commonly experienced side effects of Ruxolitinib include bruising, dizziness, headache, weight gain, high cholesterol, or gas.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"and in Appendix B: Risks of Standard of Care Procedures.***

Will being in this study help me in any way?

Our goal is to decrease the risk of GVHD after DLI and increase the chances of remission. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include that we may learn new ways of helping patients who have relapsed after a stem cell transplant.

What happens if I do not want to be in this research?

If you do not want to be in this research, your alternatives would include having a DLI with aggressive chemotherapy, having a second stem cell transplant, treatment with Decitabine or Azacitidine, or enrolling on a different research study either at the University of Minnesota or another institution. Additionally, you can choose no treatment, or comfort care.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect a total of 34 people will be in this research study. Up to 20 people will be treated here at the University of Minnesota, with the additional patients enrolled either at Washington University in St. Louis, MO or the University of Rochester in Rochester, NY.

What happens if I say "*Yes, I want to be in this research*"?

The following routine tests and evaluations will be done to determine whether or not you are eligible for this study:

- medical history
- physical exam including vital signs, height and weight
- review of your disease symptoms and use of pain medication
- routine blood tests (requiring approximately 5 tablespoons of blood) to evaluate your bone marrow, liver, and kidney function, and to check for previous viral exposure including human immunodeficiency virus (HIV), hepatitis B and hepatitis C. If your initial blood tests are abnormal, you will be notified of this and it will be recommended that a Blood Bank physician contact your personal physician regarding possible further testing. By law the Minnesota Department of Health must be notified if you test positive for hepatitis or HIV. Because of the sensitive nature of these tests, you have the right to review the results. If you have hepatitis or HIV you will not be eligible to take part in this study. You will be referred to the appropriate physicians and counselors.
- A bone marrow biopsy
- an electrocardiogram (ECG) - a test that shows the electrical activity of the heart
- any other tests or evaluations as felt needed by your study doctor
- pregnancy test

<u>Treatment Plan</u>

Unlike a bone marrow transplant, this treatment is organized in blocks of time called cycles. Each treatment cycle is four weeks long (Days 1 -28), and you may have up to another four weeks (Days 29 -56) between cycles.

Starting with the first day of the treatment, you will be asked to take the study drug, Ruxolitinib twice daily. You will continue taking this drug twice a day, every day, until six months after the end of your last cycle.

Additionally, each cycle consists of:

- Ten days of decitabine (IV infusion) in cycles 1 and 2, and five or ten days of decitabine in cycles 3 and 4
- Within two weeks of completing the decitabine, you will receive the DLI cell infusion.
- During the weeks between cycles, we will follow your recovery until you are ready to

begin another cycle. As soon as you are ready to begin the next cycle (any time between day 29 and day 56), you will be moved to the next cycle. At most, you will have four weeks between cycles.

Study calendars are attached at the end of this document as **Appendix A**.

Ruxolitinib guidelines:

- Do not crush or chew the tablets.
- You can take ruxolitinib with or without food.
- Do not drink grapefruit juice while taking ruxolitinib. Grapefruit juice can affect the amount of ruxolitinib in your bloodstream.
- If you take too much ruxolitinib call your healthcare provider or go to the nearest hospital emergency room right away. Take the bottle of ruxolitinib with you.
- If you miss a dose, take your next dose at the regular time. Do not take 2 doses at the same time.

Study Assessments

Prior to starting treatment and at specific time points after, you will be assessed in the clinic (or in the inpatient unit if you are in the hospital) to see how you are doing. During these visits you will have a clinical evaluation with a physical as well as repeating the blood tests from your pre-treatment evaluation. Prior to cycle 3 and 4-6 weeks after your last DLI/decitabine, you will have a bone marrow biopsy. At some of these visits, you will have research samples taken (see below). The timing of these visits will be as follows:

- Day 1 of each study cycle, the day of DLI in each study cycle, in between each study cycle, 4-6 weeks after the last DLI, and then every 3 months for one year after finishing the treatment.

Research Samples

In addition to the blood tests that evaluate your health, we will also take about 3 tablespoons of blood for research tests to see how your cells react to the study treatment. The timing of these labs will be as follows:

- Day 1 of each treatment cycle, 4-6 weeks after the last DLI, 90 days (+/- 7 days) after the last day of last cycle, and 180 days (+/- 14 days) after the last day of last cycle. We will also take a blood sample if your disease progresses or if you contract GVHD.

We will also take up to three samples (about 2 teaspoons each) of bone marrow. These samples will be taken at a time when you are undergoing a clinical bone marrow biopsy. One sample taken prior to cycle 3, a second sample 4-6 weeks after the last DLI. If your disease progresses, we will take a sample of bone marrow at that time as well.

Additionally, we are requesting permission to take a sample of bone marrow prior to beginning Cycle 1. Since this does not coincide with a bone marrow biopsy, it would require that you undergo this biopsy solely to collect this sample. At the end of this document, you can agree or disagree to this sample collection.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for: making sure that you take the Ruxolitinib twice daily and for coming to your scheduled clinic visits.

What happens if I say "Yes", but I change my mind later?

You can leave the research study at any time and no one will be upset by your decision.

If you decide to leave the research study, contact the investigator so that the investigator can ensure that you are no longer contacted to schedule study visits. We may ask to perform a final study assessment, if it has been more than two weeks after your last visit.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care.

If you stop being in the research, information about you that has already been collected may not be removed from the study database. You will be asked whether the investigator can collect information from your routine medical care, such as your medical records. If you agree, this information will be handled the same as the information obtained for the research study.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

DLI and Decitabine are standard treatments for post-transplant relapse of AML and MDS. Detailed risk tables are listed in **Appendix B** of this document.

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.

The sections below and in Appendix B 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 these with you.

<u>Possible Side Effects of Ruxolitinib</u>

Very Common (greater than or equal to 10%, or 10 or more out of 100 people)	**Common** (between 1 to 10%, or between 1 and 10 out of 100 people)	**Rare** (less than 1 out of 100 people)
• Bruising • Urinary tract infection • Low blood cell counts: low red blood cell counts (anemia), low platelet count (thrombocytopenia), or low neutrophil count (neutropenia)—these may make you feel more weak or tired than usual • High blood cholesterol • Hypertension • Weight gain • Constipation • Dizziness • Headache • Bleeding • Increased risk of infection such as herpes zoster (shingles), pneumonia or urinary tract infection • tuberculosis (contagious bacterial infection of the lungs)	• Flatulence/ gas • Bleeding in the digestive tract • Bleeding in the brain • Increased blood liver function tests (AST and ALT) which may indicate damage to the liver which is often reversible • Sepsis - an overactive and toxic response to an infection • Low blood cell component count - red cells, white cells, and platelets (Pancytopenia) – this may make you feel tired, short of breath, cause bruising or bleeding, or, in severe cases cause seizures, high fever, confusion or loss of consciousness	• Non-Melanoma Skin Cancer • Septic shock – dangerously low blood pressure due to sepsis, which can cause a heart failure, organ failure, stroke, or death

Frequency not reported

- Progressive multifocal leukoencephalopathy: A rare and severe viral infection of the brain, called PML, which can cause brain damage, memory loss, trouble thinking, muscle weakness, blindness, and death. Notify your study doctor immediately if you develop trouble thinking or walking, a decrease in strength in your arms or legs, or changes in your vision or hearing. This is a serious and life-threatening infection, which requires medical attention right away.

<u>Risk of Discontinuing the Study Drug - if you suddenly stop taking Ruxolitinib, you may have the following side effects:</u>

- multi-organ failure
- trouble breathing
- Disseminated Intravascular Coagulation, a condition in which blood clots form throughout your small blood vessels, which can reduce blood flow and cause organ damage

- Low blood pressure

Risk of research blood draws:
Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection.

Risk of Bone Marrow Sampling:
With the exception of the optional sample collection prior to cycle 1, we will only take a bone marrow sample when you are already having a bone marrow biopsy for clinical purposes. Taking bone marrow may be painful. The pain normally lessens within minutes to hours. Local anesthetic medications will be used to decrease the pain. There is also a small risk of infection or bleeding.

Risks of the ECG:
There is a small risk that redness or swelling could develop from the ECG electrodes (pads) that will be placed on the skin.

Risks associated with breach of confidentiality:
As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality.

At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, and marrow samples. A separate list will be maintained that will links each participant's name to the study identification number for future reference and communication.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

You should not get pregnant, breastfeed, or father a baby while in this study. Ruxolitinib could be very damaging to an unborn baby.

If you are sexually active, both men and women should use at least two effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable, but least effective, methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You might be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

Will it cost me anything to participate in this research study?

The Ruxolitinib will be provided by the study and all research samples will be paid for by study funds.

You and your insurance company will be charged for the costs of the DLI, the Decitabine, and the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

- The University of Minnesota, and the study team, research staff and medical staff as well as the study team members from Washington University (St. Louis, MO) and the University of Rochester (NY).
- Any person who provides services or oversight responsibilities in connection with this study.
- Every member of the University of Minnesota workforce who provides services in connection with this study.
- Incyte (the funder of the study) and its authorized agents. Incyte is also providing ruxolitinib for this study.
- Any laboratories, individuals, and organizations that use your health information in connection with this study.
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA), the U.S. Department of Health & Human Services (DHHS), and the Office for Human Research Protections (OHRP)).
- National and international transplant registries including the Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP)
- Other government agencies in this or other countries.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards

such as the University of Minnesota IRB, Privacy Boards, Data and Safety Monitoring Board and their related staff that have oversight responsibilities for this study.
- The Masonic Cancer Center at the University of Minnesota and/or their designee
- The Fairview BMT Outcome Database, a registry that compiles demographic and medical information related to hematopoietic cell transplant/cell therapy patients and donors

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Data or Specimens Collected
Leftover samples will be stored in labs at the University of Minnesota for future analysis. These stored specimens will be labelled only with a bar code and not contain any information that would make it possible to identify you. These samples may be stored for up to ten years.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Genetic Information
A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:
- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting

the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. The investigator(s) will not contact you or share your individual test results.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include

- If the study doctor believes, for any reason, that it is in your best interest.
- If you develop side effects that the study doctor considers unacceptable.
- If you refuse to take the study drug or return for follow-up as recommended by your study doctor, or do not follow the study doctor's instructions.
- If you refuse to have tests that are needed to determine whether the study drug is safe and effective.
- If other causes prevent you from continuing in this study.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I agree	**No, I disagree**	
_____	_____	The investigator may collect an extra bone marrow sample prior to cycle 1. I have been informed that this is a separate bone marrow collection outside of the planned biopsies for clinical care.
_____	_____	The investigator may retain any leftover blood or tissue samples taken during the study. These samples may be used for other research not related to this study. These samples will be retained in non-identifiable form, meaning that there will be no information associated with the blood or samples that will allow anyone to readily ascertain my identity.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

Signature Block for Witness:

WITNESS STATEMENT:
The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is unable to read the information
☐ The participant is visually impaired
☐ The participant is non-English speaking
☐ The participant is physically unable to sign the consent form. Please describe:
_____
☐ Other *(please specify)*:
_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:
A**s** someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____
Signature of Interpreter Date

_____
Printed Name of Interpreter

OR:

Statement from a Non-Interpreter:
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Individual Date

_____

Printed Name of Individual

Appendix A: Study Calendars

During the first two cycles, you will receive your treatment on one of the two schedules below. The only difference between these two calendars is the timing of Decitabine, which can be given either 10 days in a row, or five days in a row, followed by two days off, followed by another five days.

Calendar 1: Ten Day Dosing Schedule

Treatment	Cycle 1			Between Cycles	Cycles 2 -4			Month 1 – 6 after end of final cycle
	Day 1-10	Between Day 11-21	Day 22-28	Day 29 - 56	Day 1-10	Between Day 11-21	Day 22-28	
Decitabine	1X daily				1X daily			
DLI		One infusion				One infusion		
Ruxolitinib	2x daily →							
Health check and disease staging				X				

Calendar 2: 5/2/5 Day Dosing Schedule

Treatment	Cycle 1			Between Cycles	Cycles 2 -4			Month 1 – 6 after end of final cycle
	Day 1-5 and 8-12	Between Day 13-22	Day 23-28	Day 29 - 56	Day 1-5 and 8-12	Between Day 13-22	Day 23-28	
Decitabine	1X daily				1X daily			
DLI		One infusion				One infusion		
Ruxolitinib	2x daily →							
Health check and disease staging				X				

If after two cycles of treatment, you go into remission, your dose of Decitabine will be reduced to five days, as detailed in the calendar below. Otherwise, you will continue to receive ten doses of Decitabine as in Calendars 1 and 2.

Calendar 3: Five Day schedule for Cycles 3 and 4

Treatment	Cycle 3		Between Cycles	Cycle 4		Month 1 – 6 after end of final cycle
	Day 1-5	Between Day 6 - 16	Day 17 - 56	Day 1-5	Between Day 6-16	
Decitabine	1X daily			1X daily		
DLI		One infusion			One infusion	
Ruxolitinib	2x daily →					
Health check and disease staging			X			

In addition to the treatment, you will have visits that include lab tests to check your health and additional health assessments. The calendar below outlines the dates for this testing:

	Screening	Every Treatment Cycle		Between study cycles (day 29-56)	End of Treatment Visit	Follow-Up
		Day 1 of Decitabine	Day of DLI			
Physical exam	X	X	X		X	X
Weight (Height also during screen)	X	X				
ECG	X			X		
Clinical blood tests	X	X	X	X	X	X
Pregnancy test	X			X		
Bone Marrow biopsy	X			X (before cycle 3 only)	X (4-6 weeks after last DLI /Decitabine)	

The calendar for research samples is below:

	At Screening	Every Treatment Cycle Day 1	Prior to cycle 3 if applicable	4-6 weeks after last DLI	90 days after the last day of last cycle	180 days after the last day of last cycle	Event Driven If your disease progresses	Event Driven If you get GVHD
Blood sample (3.5 tablespoons)		X		X	X	X	X	X
bone marrow sample (2 teaspoons)	Optional (prior to cycle 1)		X	X			X	

Appendix B: Risks of Standard of Care Procedures

DLI

The major risk of infusing lymphocytes from your stem cell donor is that you will develop graft-versus-host disease (GVHD).

Acute graft-versus-disease (GVHD) mainly affects 3 organ systems:

skin	rash, redness of the skin, burning
	formation of blisters (not common), skin peeling (not common)
liver	jaundice and itching are fairly common
	serious problems with liver failure may occur
GI tract	nausea, vomiting, diarrhea, abdominal pain

Chronic graft-versus-host disease (GVHD) gives different symptoms:

> Dry eyes, dry mouth, painful mouth sores, arthritis (swollen, painful joints), skin rash, thickening of the skin, liver symptoms (similar to above), diarrhea weight loss, hair loss, lung involvement (trouble breathing), low blood counts, higher risk of infection

In the event that graft-versus-host disease is serious and requires treatment, medications including prednisone, cyclosporine, and antithymocyte globulin (ATG) may be necessary. Most of the time, GVHD can be controlled but occasionally it can be severe enough that some patients die of GVHD itself or of an infection that occurs from GVHD or its treatment. If you had mild acute or chronic GVHD following your original stem cell transplant procedure, that will not prevent you from participating in this study. Previous occurrence of severe acute and/or chronic GVHD following stem cell transplantation increases the risk of GVHD after infusion of blood "lymphocytes" from your donor. Therefore, if GVHD is currently present and requiring treatment, you cannot enter this study at this time.

A less frequent but still common problem (occurs in about 15% of patients) is failure of your bone marrow to produce blood cells called "marrow aplasia". Since the bone marrow is the blood factory, the result of this complication is a marked decrease in white blood cells, red blood cells and platelets in the blood. These can result in the same complications of low blood counts you experienced after your stem cell transplant including infections and bleeding. In the event that this occurs, we can transfuse blood and platelets but cannot efficiently replace white blood cells. Growth factors (G-CSF and GM-CSF) may be used if your white blood count is very low. Occasionally the bone marrow failure can be prolonged and rare patients have died of infection or bleeding. A few patients have required a boost of additional stem cells from their donor.

DLIs don't work in everyone and it is still possible that your cancer may not respond or relapse later.

Additional possible complications include allergic reactions to the lymphocytes present in the

blood cells obtained from your donor. These are rare.

Your doctors will observe you carefully for these or any other problems that may develop and will provide prompt medical treatment for any complication which may occur.

Decitabine

Decitabine		
Very Common (greater than or equal to 10%, or 10 or more out of 100 people)	Common (between 1 to 10%, or between 1 and 10 out of 100 people)	Rare (less than 1 out of 100 people)
• low platelet count with increased risk of bruising/bleeding • low white blood cell count with increased risk of infection • low red blood cell count (anemia) with symptoms like tiredness, low energy, or shortness of breath • nausea • vomiting • diarrhea • constipation • tiredness • fever • pain or swelling in the arms or legs	• blurred vision • pain • high blood sugar • headache • bruises or bleeding • swollen lymph nodes ("glands") • sores in mouth, on tongue, or on lips • infection • indigestion or sour stomach • abnormal blood tests which suggest that the drug is affecting the liver • fluid build-up around the heart (congestive heart failure) • bone pain	• confusion • trouble sleeping • fluid in the lungs • severe allergic reaction, with symptoms like flushing, hives, trouble breathing or swallowing, dizziness, swelling of mouth or throat (while drug is being infused) • serious infections • death from infection, bleeding, or other cause • damage to the kidneys • fast or irregular heartbeat • heart attack • blood clot in the lungs • inflammatory rash and skin lesions on the arms, neck, head and trunk