The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	**A Phase I/II, Open-Label, Multi-Center Study Evaluating the Safety and Efficacy of Ruxolitinib and CPX-351 in Combination for the Treatment of Advanced Phase Myeloproliferative Neoplasms**
Principal Investigator:	**Uma Borate, MD**
Sponsor:	**The Ohio State University**
Funding Sponsors:	**Incyte Corporation** **Jazz Pharmaceuticals, Inc**

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

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

We are asking you to take part in a clinical trial, a type of research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

In this clinical trial we are studying myeloproliferative neoplasms (MPN) that are transforming or have transformed into acute myeloid leukemia (AML), a cancer of the blood which usually results in rapid growth of abnormal white blood cells. These stages of disease are referred to as MPN-accelerated phase (MPN-AP) or MPN-blast (immature blood cancer cell) phase (MPN-BP). MPN-BP is also referred to as "secondary AML" because that type of AML was proceeded by an MPN. In this study, you will be given a drug called, ruxolitinib, after you receive standard of care induction with CPX-351. CPX-351 is a combination of two chemotherapy drugs, daunorubicin and cytarabine.

Medical personnel who carry out research studies are called "investigators." The investigator will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You can discuss your decision with your friends and family. You can also discuss it with your health care team or another doctor. If you have any questions, ask the investigator.

1. Why is this study being done?

This study is being done to answer the following question:

Can we treat your MPN-AP MPN-BP and reduce symptoms of your disease by adding a new drug to the usual combination of drugs?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your disease. The usual approach is defined as care most people get.

In this study, we will learn about a drug called ruxolitinib. We do not know if ruxolitinib works. Ruxolitinib has been approved by the FDA for MPNs but not for the conditions being studied, MPN-AP and MPN-BP.

2. How many people will take part in this study?

As many as 47 people will take part in this study, which will be conducted at Ohio State University and 4 other universities around the country. Of these participants, we expect 22 will be screened at OSU.

3. What will happen if I take part in this study?

Before you begin the study:

You will need to have the following: medical history reviewed, physical exam, spleen assessment, electrocardiogram (ECG), chest X-ray, urine sample, echocardiogram (ECHO) or MUGA scan, blood labs, pregnancy test if applicable, and bone marrow exam to find out if you can be in the study. If you need subsequent cycles of study treatment (re-induction or consolidation), a physical exam, pregnancy test if applicable, labs and possibly a bone marrow exam will be necessary.

During the study:

Treatment cycle lengths will vary depending on the type of therapy you are receiving. Induction and re-induction cycles will be up to 28 days, but may be shorter than 28 days. Consolidation cycles will be 28 days.

- You will complete standard of care induction, CPX-351 on Days 1, 3, and 5 and then on Day 6 you will receive ruxolitinib for approximately 23 days.
- If applicable, you will complete standard of care re-induction, CPX-351 on Days 1, and 3 and then on Day 4 you will receive ruxolitinib for approximately 25 days.
- If applicable, you will complete standard of care consolidation, CPX-351 on Days 1, and 3 and then on Day 4 you will receive ruxolitinib for approximately 25 days.
- If applicable, you will complete up to 8 cycles of maintenance therapy where you receive the ruxolitinib on days 1-28.

The ruxolitinib tablets should be taken twice daily, and should be swallowed whole. You will take ruxolitinib at approximately the same time each day. If you forget to take ruxolitinib, do not replace your missed dose. If you are unable to take the pills by mouth the drug will be held. You will be asked to complete a drug diary to record when you take ruxolitinib. This document can help you keep track of when you've taken the drug as well as tell the investigator how many doses you took. While you are in the hospital, you may not be asked to complete it since the nurses will record the doses in the medical record system.

You will have the following tests and procedures. They are part of regular cancer care.

- Physical examination
- Vital signs (weight, blood pressure, pulse, body temperature)
- Spleen assessments
- Urinalysis
- Blood draw (about 1.5 teaspoons) for standard laboratory tests
- Blood draw (about 1.5 teaspoons) for restaging of your disease
- Bone marrow biopsy on recovery of blood counts to assess your disease response (one time between days 35-42)
- Bone marrow biopsy again only if needed (your provider will decide)

You will have these tests and procedures that are either being tested in the study or being done to see how the study is affecting your body.

- Collection of research samples from bone marrow aspirate and biopsy.

Please see the study calendars at the end of this form for more information.

When you are finished taking the ruxolitinib:

If your disease gets worse or if you are unable to tolerate the ruxolitinib, you will be taken off the study.
If you have any questions regarding this study now or in the future, contact Dr. Uma Borate at (503) 494-5058.

It is extremely important that you, any caregivers, and other healthcare providers have the correct study team contact information for safety and management of toxicities. To address this, Trial Alert Cards have been created to record study team phone numbers, with a 24-hour option, and come in a size that can be carried in your wallet. The cards include a note to healthcare providers asking them to contact your treating physician, in case you seek care with anyone unfamiliar with the trial. You will receive this card at your first/ next visit, please keep it with you at all times.

4. How long will I be in the study?

Research procedures will take place during your standard of care visits and will not involve an additional time commitment.

You will be asked to take ruxolitinib for up to 25 days following standard of care induction, re-induction, or consolidation. If you are benefiting from treatment, you may continue for up to approximately 1 year total.

After you have finished study treatment, you will be asked to visit the office for a follow-up exam within 30 days of stopping. You will then be asked to visit the office for follow-up visits every 2 months for 1 year or until you start of a new treatment (whichever occurs first).

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

If you wish to withdraw from the study, please contact the principal investigator, Dr. Uma Borate, at:

Uma Borate, MD
2121 Kenny Road

Columbus, OH 43210
Ph:614-685-9828
Email: Uma.Borate@osumc.edu

6. What risks, side effects or discomforts can I expect from being in the study?

PHYSICAL RISKS

Ruxolitinib may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The investigator will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from ruxolitinib.

The risks of the standard of care induction with CPX-351 are known. The side effects of treatment with the standard of care drugs followed by ruxolitinib are not known and may include additional side effects, including death.

Here are important points about side effects:

- The investigators 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.
- You may have some side effects we do not expect because we are still learning about ruxolitinib for MPN-AP and MPN-BP.
- *There may be unanticipated risk to an embryo or fetus if you or your partner becomes pregnant.*
- You may not have symptoms for some of these side effects, but you will be monitored by the investigator to check for any changes throughout the study.

Here are important points about how you and the investigator can manage side effects less:

- Tell the investigator if you notice or feel anything different so they can see if you are having a side effect.
- The investigator may be able to treat some side effects.
- The investigator may adjust the drugs used in this study to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the investigator will discuss these with you.

Patients with diagnosed MPN-AP and MPN-BP

The possible effects for the combination of standard of care CPX-351 and ruxolitinib are unknown It's possible that using these drugs in combination could increase the severity and/or likelihood of experiencing the side effects associated with each drug.

The possible reported side effects of ruxolitinib are as follows:

SEEN IN OVER 10% OF PEOPLE USING RUXOLITINIB
Some may be serious

- Thrombocytopenia or decreased blood platelets (elements in the blood that assist in blood clotting), which can lead to bleeding and bruising
- Anemia, or low red blood cells, which can lead to making you feel tired, short of breath, put extra strain on your heart, and may require a blood transfusion to treat
- Neutropenia or decreased neutrophils (a type of white blood cell that helps your immune system fight infections), which can increase your risk of developing infections
- Bruising
- Dizziness
- Headache
- Increased liver enzymes (proteins in the liver that could indicate liver damage)
- High cholesterol, which can lead to chest pain, blood clots, heart attack, or stroke
- High triglycerides, which is symptomless but can lead to pancreatitis. Symptoms of pancreatitis include abdominal pain, back pain, nausea, vomiting, shortness of breath, or skin problems.
- Infections of the urinary tract or bladder which can lead to pain with urination, frequent urination, back pain, lower abdomen pain, feeling tired, fever, or chills
- Weight gain
- Nausea
- Diarrhea
- Vomiting
- Fatigue (feeling tired)
- Edema (mild swelling usually of the hands and feet)
- Impaired kidney function (increased blood creatinine)
- Constipation

SEEN IN OVER 10% OF PEOPLE USING RUXOLITINIB *Some may be serious*
• Increase in blood pressure causing hypertension • Herpes zoster (also known as shingles, a viral infection that causes a painful skin rash with blisters, usually occurring in a limited area on one side of the body)

SEEN IN LESS THAN 10% OF PEOPLE USING RUXOLITINIB

Some may be serious

- Gas or Flatulence
- Weakness
- Low to moderate-grade fever
- Feeling hot
- Tingling or pain in the hands or feet
- Anxiety
- Insomnia (difficulty sleeping)
- Shortness of breath
- Increased heart rate or irregular heartbeat
- Heart murmur (extra or unusual sound heard during a heartbeat). Symptoms may include: shortness of breath, chest pain or dizziness)
- High-grade fever
- Significantly low platelets
- Moderate anxiety
- Significant insomnia
- Chills
- Night Sweats
- Sore Throat
- Sinusitis
- Muscle Pain
- Low oxygen level (which can cause shortness of breath and fatigue)
- Inflammation of the lungs (which can cause shortness of breath and dry cough)
- Eye damage or disorder (which may cause eye pain or changes in vision)
- Tuberculosis, an infectious disease spread through the air. Tell your doctor immediately if you have any of these symptoms: chronic cough, blood in sputum, fever, night sweats and weight loss.
- Non-melanoma skin cancers (NMSCs) have been reported in patient taking ruxolitinib for other diseases. NMSCs are skin cancers such as basal cell cancer or squamous cell cancer that usually develop on the sun-exposed areas of skin, and commonly require surgery to remove. It is not known whether or not ruxolitinib contributed to these cases of NMSC.
- The amount of Hepatitis B (HBV) detected in blood has been reported to increase in patients with chronic HBV while taking ruxolitinib. The effect of ruxolitinib on patients with chronic HBV is unknown.
- Pneumonia

Rare but serious

- A rare disease called progressive multifocal leukoencephalopathy (PML) has been reported during ruxolitinib treatment. PML comes from a viral infection that causes brain damage and can be fatal. It is unknown whether this was due to ruxolitinib treatment since PML has occurred in patients with blood cancers, including MF, who were not treated with ruxolitinib. Tell your doctor immediately if you have any of these symptoms: confusion or problems thinking, loss of balance or problems walking, clumsiness, difficulty speaking, decreased strength or weakness on one side of your body, blurred and/or loss of vision.
- Fatal intracerebral hemorrhage (bleeding in the brain or stroke)
- Fatal cardiac arrest (heart attack)
- Development of secondary cancer, such as lymphoma or chronic myelogenous leukemia (CML).
- Severe Edema (fluid buildup in the arms, legs, hands, feet, lungs, heart, head, and abdomen) that can cause swelling, pain, shortness of breath, fullness, and weakness
- Pancytopenia (low platelets, low red blood cells and low white blood cells at the same time)
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There may be risks associated with the discontinuation of the study medication. Patients who have symptomatic heart or lung disease might experience serious and life-threatening worsening of their heart or lung condition when the ruxolitinib is stopped. Therefore, it is important that you inform your doctor about any history of heart or lung disease, and if you stop taking your medication for any reason and develop worsening of your symptoms, tell your doctor right away. Other risks that might be related to stopping the ruxolitinib include inflammation, acute response to drug withdrawal (which can cause anxiety, sleep loss, or weakness) and recurrences of signs and symptoms of your disease (including rapid increase in spleen size). You should tell the study doctor if you experience any of these symptoms when you stop taking ruxolitinib.

The possible reported side effects of CPX-351 are as follows:

SEEN IN OVER 10% OF PEOPLE USING CPX-351 *Some may be serious*
• Skin Rash • Fever and Infections (Febrile Neutropenia, bacteraemia) • Pneumonia • Nausea and Diarrhea • Musculoskeletal Pain (pain in the muscles and/or joints) • Constipation • Fatigue • Fever (Pyrexia) • Chills • General Swelling • Reduced Appetite • Vomiting • Cough • Headache • Shortness of Breath • Nosebleed • Mouth Sores and Mouth Swelling • Low Potassium (which may cause weakness) • Small Red or Purple Skin Spots • Dizziness • Low Blood Pressure • Anxiety • Stomach Pain • Insomnia • Skin Itching • Hypersensitivity to study drugs • Fast Heart Rate • Weakness • Arm and Leg Swelling • High Blood Pressure

SEEN IN LESS THAN 10% OF PEOPLE USING CPX-351 *Some may be serious*
• Bleeding in the Brain • Blood Infection (sepsis and septic shock) • Decreased Heart Function • Heart Failure • Heart Attack (Myocardial Infarction) • Respiratory Failure • Seizures

Please note that these percentages are provided by the drug manufacturer for use of the drugs by themselves, but may not reflect risk using in combination with each other.

Risk of Brain Bleeding

At OSU, we have had an increased number of patients experience bleeding in the brain related to CPX-351 than is noted above. There is a possibility the combination of CPX-351 and ruxolitinib could put you at higher risk of brain bleeding than the individual drug risk, although the chance of this occurring is unknown. We felt it important to let you know about the possibility of the higher risk, but this doesn't mean that the above drug manufacturer information is incorrect or that there's a greater risk at OSU specifically.

Infusion-Associated Reaction Risk

The CPX-351 is given as an infusion through a vein. In large clinical trials of patients receiving liposome encapsulated chemotherapy by injection, some acute infusion-associated reactions were observed. Infusion-associated reactions have been very rare after CPX-351 and signs and symptoms include: flushing; shortness of breath; headache; chills; back pain; tightness in the chest; and low blood pressure. In most patients, these reactions resolved over several hours to 1 day once the infusion was completed. In some patients, the reaction stopped when the speed of the drug being given was slowed down.

There is a risk of the drug, daunorubicin, leaking out of the vein during an infusion or injection. This is referred to as "local tissue necrosis (death) after extravasation" and may cause serious damage to local tissues. Daunorubicin is contained within the CPX- 351 liposome and local tissue necrosis after extravasation is considered possible but unlikely.

Because CPX-351 contains copper it should not be administered to patients with Wilson's disease or any other disorder of copper metabolism (absorption, processing or excretion). During the study, your nurse or doctor may draw blood to watch your copper levels.

What about birth control and pregnancy during the study?
If you are a woman:

- Taking part in the study might harm your fetus or breastfed baby. You cannot take part in this study if you are pregnant or breastfeeding a child.
- You must agree not to become pregnant while you are in this study.
- If you are sexually active and able to get pregnant you must use two birth control methods that can either be two barrier methods or a barrier method plus a hormonal method to prevent pregnancy during the study and for 6 months after your last dose. Your study doctor will review birth control methods that can be used while in this study. The study doctor must approve the method you use before you can enter the study.
- If you get pregnant during the study, you must tell the study doctor immediately. You will have to stop study treatment. The study doctor will advise you about your medical care and will ask you to allow him/her to collect information about your pregnancy and the health of your baby.

- If you become pregnant within 6 months after your last dose, you must tell the study doctor immediately. The sponsor, OSU, may ask you to allow them to collect information about her pregnancy and the health of the baby.

If you are a man:

- The effect of the study treatment on your sperm is unknown.
- From when you start taking the study treatment until 6 months after your last dose, you must use a condom with spermicidal when you have sex. You must not donate sperm during the study and for 90 days after your last dose of study treatment.
- If your partner becomes pregnant in the time between when you start taking study treatment until 6 months after your last dose, you must tell the study doctor immediately. The sponsor, OSU, may ask you and your partner to allow them to collect information about her pregnancy and the health of the baby.

The following procedures are standard of care and involve clinical risks described below. The risk associated with taking additional samples (bone marrow and blood draw) for research purposes is not known:

Blood draw*:* We will draw blood from a vein in your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, or an infection.

X-rays: In this study, you will be exposed to radiation during the chest x-ray. While we cannot be sure any dose of radiation is entirely safe, the amount you will be exposed to in this study is not known to cause health problems.

Bone marrow biopsy: Bone marrow biopsy means taking some cells from inside your bones. To do this, we will numb an area of your skin (usually near your hip) with a shot. The shot may cause a little pain. Some people (fewer than 1 in 10,000) are allergic to the shot you will get to numb the area. Then we will insert a long needle into your bone to get the cells. Some people have moderate to severe pain when the bone marrow cells are drawn in through the long needle. Your hip may hurt for about 3-6 days. There is a small chance you will get a bruise or an infection where the needle will be inserted. You may bleed or have a scar. Your skin may itch. These problems are rare.

Potential drug interactions: There are several drugs (prescription and non-prescription) that may cause problems when taken with ruxolitinib. The investigator will carefully review all of the drugs you are taking before giving you ruxolitinib. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the investigator before you take the new drug. You could also have that provider talk to the investigator before prescribing the new drug. Do not take any new over-the-counter drugs while you are in this study unless you first check with the investigator.

OTHER TYPES OF RISKS

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.
- The targeted study drug chosen for you by the investigational drug screen test may not be better, and could possibly be worse, than the usual approach for your cancer.
- The targeted study drug chosen for you or the dose you receive may not be effective in helping to treat your disease. This means you may spend time in the study and experience side effects taking a drug that may not provide you with any health-related benefits.
- You may be withdrawn if you do not follow the instructions given to you by the investigator.

7. What benefits can I expect from being in the study?

You may or may not personally benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

If you decide not to take part in this study, you do have other choices. For example:

- You may choose to have standard treatment for your cancer (7+3 chemotherapy or CPX-351)
- You may choose to take part in a different study, if one is available
- You may choose to have no treatment

If you decide that you do not want any further active treatment for your cancer, one of your options is called "comfort care." Comfort care means that your doctor will offer you medication to help control your pain, together with any other treatment and support you need to help you maintain your overall comfort and dignity. It is often possible for this comfort care to be provided at home. If you think that comfort care is something you might prefer, feel free to discuss it with family and friends, any spiritual advisor, and of course, your doctor. Please take your time to make a decision whether you would like to take part in this research study. Feel free to discuss it with your family and friends.

9. What are the costs of taking part in this study?

The drugs ruxolitinib and CPX-351 will be provided at no cost to you while you participate in this study. Tests and procedures performed solely for research purposes will be provided at no cost to you. This includes but is not limited to: on treatment imaging of your abdomen/spleen and research testing on your tissue and blood by a central lab. Your study doctor or coordinator can tell you, specifically, which costs are covered by the study.

Most of the care you receive during this study is considered routine for your disease. Routine costs include: hospital stays (if needed), doctors' fees, lab work, baseline imaging of your abdomen/spleen. This may include the costs of care and treatment of any side effects or complications resulting from your participation in this study. The costs of routine medical care will be billed to you and your insurance provider in the usual manner. You will be responsible for any deductibles, coinsurance or copayments required by your particular plan. You may be responsible for any costs not paid by your insurance provider.
If you are a Medicare Advantage Plan participant (HMO or PPO), original Medicare is billed first for routine, study-related services while you participate in an approved trial. Your Advantage Plan is billed second for their share of your costs. You may or may not have additional out of pocket costs after Medicare or your Advantage Plan pays. Additional information can be obtained from your Advantage Plan and online at:

https://www.medicare.gov/Pubs/pdf/02226-Medicare-and-Clinical-Research-Studies.pdf

Some insurance providers will not pay for routine costs if you are participating in a research study. Others may limit what they pay or where you can receive care. Before participating in this study, we recommend that you ask your insurance provider if there are any limitations to your particular plan. Otherwise, you might experience unexpected medical costs. A financial counselor is available on request.

10. Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

Reimbursement for travel related to the study is not available.

11. What happens if I am injured because I took part in this study?

OHIO STATE UNIVERSITY LIABILITY
If you are injured as a result of your participation in this study, you may obtain immediate care at the Ohio State University Medical Center. The cost of this treatment will be charged to you or your insurance company. Your health insurance company may or may not pay for treatment of injuries as a result of your participation in this study. The Ohio State University has no funding set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, it/they may be used or shared with other researchers without your additional informed consent.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find information that significantly and directly impacts your health, we will share it with you. This information will be shared by your treating physician.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  Sexually transmitted diseases
  Other reportable infectious diseases
- Records about any study drug you received;
- Records about the study device; and

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Others: The sponsors, Jazz Pharmaceuticals and Incyte Corporation

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact**:**

Uma Borate, MD
2121 Kenny Road
Columbus, OH 43210
Ph:614-685-9828 Uma.Borate@osumc.edu

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact 614-293-4477, privacyoffice@osumc.edu or by mail at:

HIPAA Privacy Officer

650 Ackerman Rd.
Columbus, OH, 43202

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact**:**

Uma Borate, MD
2121 Kenny Road
Columbus, OH 43210
Ph:614-685-9828 Uma.Borate@osumc.edu

Study Calendars

Schedule of Procedures and Evaluations for Induction Therapy with CPX-351 and ruxolitinib																																
				Treatment Period																												
				Induction 1 and 2 (Days)																												
Visit Days (± 3 Days)		Screen	Baseline	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29-42**
Treatment Administration	CPX-351			X		X		X[A]																								
	Ruxolitinib								X[B]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Informed consent and eligibility assessment		X																														
Medical history/ medication review		X		X																											X	
Physical Examination		X	X	X													X														X	
Spleen assessment			X																													
Chest X-ray/CT Scan			X																													
ECG			X																													
ECHO/MUGA Scan			X																													
Blood Sampling			X	X		X		X		X		X		X		X	X	X		X		X		X		X		X			X	
Urine Sampling			X	X																												
Pregnancy test (if applicable)			X																												X	
Bone Marrow Exam			X																													X
Response Assessments																																X
Side Effect Assessment			X	X----------X																												

[A] CPX-351 is given on day 5 for initial induction only (not for re-induction).
[B] Ruxolitinib is started on day 6 of initial induction only (ruxolitinib will be administered starting on day 4 for re-induction)

Schedule of Procedures and Evaluations for Consolidation Therapy with CPX-351 and ruxolitinib																													
		Treatment Period																											
		Consolidation 1 and 2 (Days)																											
Visit Days (± 3 Days)		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**
Treatment Administration	CPX-351	X		X																									
	Ruxolitinib				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Medication review																													X
Physical examination															X														X
Blood Sampling		X		X		X									X														
ECHO/MUGA Scan		X																											
Pregnancy test (if applicable)		X													X														
Bone marrow exam																													X
Response assessments																													X
Side Effect Assessment		X----------																											----------X

Schedule of Procedures and Evaluations for Maintenance Therapy with Ruxolitinib																													
		Maintenance Treatment Period Up to 8 Cycles (Days)																											
Visit Days (± 3 Days)		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**
Treatment Administration	Ruxolitinib	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Medication review																													X
Physical Examination		X													X														X
Blood Sampling		X													X														X
Bone Marrow Exam																													X[F]
Response Assessments																													X
		X----------X																											

	Schedule of Procedures and Evaluations for End of Treatment and Follow-up (does not apply to transplant participants)							
Visit Days (± 10 Days)	**EOT**	**Follow-up (months)**						
		1	**3**	**5**	**6**	**7**	**9**	**12**
Participant status (can be by phone)	X	X	X	X		X	X	X
Blood Sampling	X	X	X	X	X (if applicable)	X	X	X
Bone Marrow Exam	X		X----------X					
Side Effect Assessment	X	X			X			

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant** **Date and time** **AM/PM**
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**Date and time** **AM/PM**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent** **Date and time** **AM/PM**

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness** **Date and time** **AM/PM**
Printed name of witness	**Signature of witness** **Date and time** **AM/PM**