PATIENT INFORMATION SHEET
Phase 1/2 Study

Study Title: The ABNL-MARRO 001 Study: A Phase 1/2 Study of Active Myeloid Target Compound Combinations in MDS/MPN Overlap Syndromes

Key Information

This study is for research purposes, participation is voluntary
You are being asked to take part in a research study. Research studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.

Purpose, duration, overview of study
This study will investigate whether a new experimental treatment, ASTX727 with itacitinib, will be a safe and possibly effective treatment option for patients with Myelodysplastic syndrome/Myeloproliferative Neoplasm Overlap Syndromes (MDS/MPN).

ASTX727 and itacitinib will be self-administered (by mouth) in clinic under direct observation of the clinical staff on Days 1, 2, 3, 4 and 5 of treatment cycle 1 in Phase 1, and Days 1, 3, and 5 of treatment cycle 1 in Phase 2, and then again on Day 1 of treatment cycle 2 (phase 1 only), cycle 3 and cycle 7. A treatment cycle is 28-days long.

You may continue to receive study treatment for up to 12 months, as long as you are tolerating the treatment and your doctor determines that you are benefiting from the treatment. During each cycle you will undergo tests and procedures. They are part of regular cancer care. Some tests and procedures will be needed more often than normal because you are in this study. You will also have some of these tests and procedures performed no later than 16 days after you stop taking the study treatment. A follow-up call to discuss the state of your disease will take place every 3 months after your final treatment on study for a maximum of 1 year.

Reasonable, foreseeable risks or discomforts
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your doctor may give you medicines to help lessen side effects. Many side effects disappear soon after you stop receiving the study treatment. In some cases, side effects can be serious, long lasting, or may never go away.

The most common side effects observed in studies with ASTX727 (occurring in ≥10% of patients) included:

- low blood platelet count
- low levels of neutrophils (a type of white blood cell) in the blood
- low levels of red blood cells
- low levels of neutrophils in the blood associated with fever
- low levels of leukocytes (a type of white blood cell) in the blood
- constipation and/or abdominal pain
- nausea, vomiting, and diarrhea

- extreme tiredness
- low appetite and weight loss
- infection in the mouth, throat, or skin
- infection or inflammation of the lungs called pneumonia, associated with cough and/or shortness of breath
- inflammation of the mucous membrane of the mouth
- urinary tract infection
- fever with or without chills
- bleeding from the nose, mouth, skin, urinary bladder, stomach
- swelling due to fluid buildup
- increase in liver enzymes
- increased levels of a waste product called creatinine
- high blood sugar
- abnormal, fast, or irregular heartbeat
- generalized aches and pains
- skin rash
- trouble sleeping
- dizziness
- low blood pressure

The most common side effects observed in studies with itacitinib (occurring in ≥10% of patients) included:

- low red blood cell count
- extreme tiredness
- low blood platelet count
- upper respiratory tract infection
- nausea
- diarrhea
- constipation
- cough
- swelling due to fluid buildup
- fever
- dizziness
- shortness of breath
- abdominal pain
- joint pain
- limb pain
- rash
- bruising
- headache
- night sweats
- skin itching
- back pain
- vomiting
- nose bleeds
- fall
- low appetite
- high blood pressure
- pneumonia

- muscle spasm

Potential benefits
There may be no direct benefits to you from participating in this study. However, the information gained from this study may help doctors learn more about ASTX727 in combination with itacitinib for the treatment of MDS/MPN. This information could help other people with cancer in the future.

Alternatives to this research study
If you decide not to participate in this study, your other choices may include:

- Receiving treatment with other cancer drugs that have been approved for treatment of MDS/MPN in the United States.
- Taking part in another clinical study
- Getting no treatment/getting palliative care

INFORMED CONSENT DOCUMENT FOR RESEARCH

Study Title The ABNL-MARRO 001 Study: A Phase 1/2 Study of Active Myeloid Target Compound Combinations in MDS/MPN Overlap Syndromes

Study Doctor Dr. Michael R Savona

This informed consent applies to:

Name of participant: _____ Age: _____

This informed consent document is being given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

1. What is the purpose of this study?

You are being asked to take part in this research study because you have been diagnosed with Myelodysplastic syndrome/Myeloproliferative Neoplasm Overlap Syndromes (MDS/MPN) and require treatment.

This study involves investigational drugs. An investigational drug is one that has not been approved by the Food and Drug Administration (FDA) for your disease. The combination of drugs in this study is investigational.

Vanderbilt University Medical Center and Theradex Oncology are sponsoring the study. Astex Pharmaceuticals, Inc. is providing the study drug ASTX727. Incyte Corporation is providing the other study drug: Itacitinib. The doctor in charge of this study is Dr. Michael Savona.

The purpose of this study is to learn:

- What dose of the combination of ASTX727 with itacitinib is safe and tolerable for human patients, and
- Whether the response to the combination of ASTX727 with itacitinib warrants further investigation in other trials.

This study has a Phase 1b dose escalation phase and a Phase 2 expansion phase. The first phase, Phase 1b focuses on the safety of combining the two investigational drugs and determining a safe and tolerable dose and treatment schedule of the combination therapy to use in Phase 2. The dose of ASTX727 and itacitinib that a patient receives during Phase 1b will depend on the doses being examined within the patient treatment cohort at the time of study enrollment. Phase 1b will include participants who have either had no treatment at all or who have relapsed or are not responding to treatment for MDS/MPN. Phase 2 focuses on the effectiveness of the drug combination when used at the dose and treatment schedule chosen in Phase 1b and enrolls patients in two stages. Only participants who have had no prior treatment for MDS/MPN will be included in the first stage of Phase 2. In the second stage of Phase 2, participants who have either had no treatment at all or who have relapsed or are not responding to treatment will be included.

Before signing this informed consent document, the study doctor will talk to you about other treatments or therapies that are available. These other treatments/therapies may already be approved for your condition or there may be other study drugs in different clinical studies available to you. There may be different opinions as to whether these other treatments would be good for you. It is important that you talk to the study doctor about the benefits/risks of all treatment options.

2. How many people will take part?

A minimum of 6 patients and maximum of 30 patients will be treated during Phase 1b testing of ASTX727 in combination with itacitinib. In Stage 1 of Phase 2, a minimum of 20 patients who have not previously received MDS/MPN treatment will be treated at the dose and schedule chosen in Phase 1b. If the dose is deemed safe and effective, an additional 38 patients who have not previously received treatment and 29 patients who have relapsed or are not responding to treatment will be treated in Stage 2 of Phase 2.

3. Do I have to take part?

You do not have to take part in this research study. You may choose not to be in this study and receive other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time and for any reason. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether you still want to be in this study. Your medical record will contain a note confirming you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

4. What will happen to me if I decide to take part?

The below text summarizes the visits, tests and procedures required as part of the study.

Screening Visit (14 days to 1 day before start of treatment)
After you sign the informed consent form, your study doctor will check your eligibility for the study. During this visit, you will be asked about your medical history, quality of life and general health, including what medications you are taking. You will also undergo different tests and examinations including, safety blood tests, physical examination (including assessment of the liver and spleen), assessment of vital signs, height and weight, pregnancy test (for women of childbearing potential), and a recording of the electrical activity of the heart (electrocardiogram). A CT scan of the abdomen will be done, and blood samples and a bone marrow biopsy and aspirate will be obtained to determine response (or for future exploratory research).

Cycle 1 (consists of visits on Days 1, 2, 3, 4, 5, 15 and 22)
If you are eligible for study participation you will enter the treatment phase. Each treatment cycle is 28 days long. Cycle 1 consists of 7 different visits with ASTX727 and itacitinib self-administered on Days 1, 2, 3, 4 and 5.

On these days, you will self-administer the ASTX727 and itacitinib pills in clinic under direct observation of the clinical staff. On the remaining days of the cycle, you will self-administer itacitinib pills at home through Day 28 as instructed by your study doctor. You will need to refrain from eating for 2 hours before and 2 hours after ASTX727 and itacitinib administration.

Itacitinib is known to affect the immune system. An increased incidence of infections could possibly occur. Subjects receiving itacitinib will also receive treatment to help prevent infection with Pneumocystitis, which can result in pneumonia, for the duration of study treatment and for at least 60 days after the last dose of study treatment.

The following tests and procedures will be performed on Day 1 of Cycle 1: physical examination (including assessment of the liver and spleen), vital signs assessment, measurement of weight, safety blood tests, an electrocardiogram, a pregnancy test (for women of childbearing potential), one blood sample at several timepoints will be collected for an assessment of what the body does to the drugs (pharmacokinetics) for up to 4 hours after administration of ASTX727 and itacitinib, and questions will be asked about your general well-being, quality of life, any medications you are taking, and any side effects you may be experiencing.

- Vital signs assessments will also be carried out at each of the remaining visits in Cycle 1.
- One blood sample for pharmacokinetic assessments will be taken again on Day 2 and 5 before the administration of ASTX727 and itacitinib.
- An electrocardiogram will be performed again on Days 3 and 5,
- Safety blood tests will be performed again on Days 3, 5, 15 and 22.
- Questions will be asked about any side effects you may be experiencing on Days 5, 15 and 22.
- Physical examination will be performed on Days 15 and 22.

Cycle 2 (consists of visit on Day 1 and Day 15)
You will self-administer the ASTX727 and itacitinib pills in clinic under direct observation of the clinical staff on Day 1 of Cycle 2.

The following tests and procedures will be performed on Day 1 of Cycle 2: physical examination, vital signs assessment, measurement of weight, safety blood tests, an electrocardiogram, a pregnancy test (for women of childbearing potential), blood samples pharmacokinetic assessments, and questions will be asked about your general well-being, quality of life, any medications you are taking, and any side effects you may be experiencing.

On Day 15 of Cycle 2 you will undergo a physical examination, vital signs assessments, safety blood tests, and you will be asked questions about any side effects you may be experiencing.

Cycle 3 onwards (Day 1)
You will self-administer the ASTX727 and itacitinib pills in clinic under direct observation of the clinical staff on Day 1 of Cycle 3 and cycle 7.

The following tests and procedures will be performed on Day 1 of Cycle 3 and all subsequent cycles: physical examination (with assessment of the liver and spleen on Day 1 of Cycles 3 and 7 only), vital signs assessment, measurement of weight, safety blood tests, a pregnancy test (for women of childbearing potential), and questions will be asked about your general well-being, any medications you are taking, and any side effects you may be experiencing.

The following tests and procedures will be performed on Day 1 of Cycles 3 and 7: a CT scan of the abdomen, blood samples and a bone marrow biopsy and aspirate obtained for determining response (or for future exploratory research), and questions will be asked about your quality of life.

End of Treatment visit
The end of treatment (EOT) visit will occur no later than 16 days after yours or your study doctor's decision to permanently discontinue treatment and prior to you starting any new anti-cancer therapy. The following tests and procedures will be performed at the EOT visit: physical examination (including assessment of the liver and spleen), vital signs assessment, measurement of weight, safety blood tests, an electrocardiogram, a CT scan of the abdomen, blood samples and a bone marrow biopsy and aspirate

obtained for determining response (or for future exploratory research), and questions will be asked about your general well-being, quality of life, any medications you are taking, and any side effects you may be experiencing.

Follow-up visit
A follow-up visit will occur 30 days (+14 days) after your final treatment on study. The following tests and procedures will be performed at the follow-up visit: physical examination (including assessment of the liver and spleen), vital signs assessment, measurement of weight, safety blood tests, and questions will be asked about your general well-being, any medications you are taking, and any side effects you may be experiencing.

Survival Follow-Up
If you agree, you will be followed up for survival every 3 months (±14 days) after your final treatment on study, for a maximum of 1 year.

Phase 2
The assessments performed in Phase 2 are the same as those described above, except for the following:

- There are no Day 2 and Day 4 visits in Cycle 1 of Phase 2
- ASTX727 and itacitinib pills will not be administered under direct observation of the clinical staff on Day 1 of Cycle 2
- Samples for pharmacokinetic assessments are not taken in Phase 2
- An electrocardiogram is not performed on Day 3 of Cycle 1 in Phase 2
- A pregnancy test is only required at screening and in Cycle 1, not in subsequent cycles of Phase 2

5. What do I have to do?

You will be asked to visit your clinic for a screening visit, to determine if you are eligible for the study, and to return for days 1-5, 15 and 22 of the first month of treatment. In the second month of treatment, you will return for two days, and for one day from the third month onwards. You will be asked to return to the clinic for procedures for each visit until the end of the study period or if you and/or your study doctor decide to remove you from the study for any reason.

6. How long will I be in the study?

Your participation in this study is expected to last about 12 months. It is anticipated that you will receive study treatment until your disease progresses, the treatment becomes unacceptably toxic, you withdraw your consent, or you do not fulfill reasonable study requirements.

7. Can I stop being in the study?

You can decide to stop at any time. It is important to tell your study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. It may be necessary for you to have certain tests or procedures if you decide to stop, to ensure your safety. Your study doctor will discuss with you what follow-up care and testing could be most helpful to you.

The study doctor may remove you from the study without your consent for any of the following reasons:

- if it appears to be medically harmful to you,
- if you do not do what the study doctor or the study staff tells you to do,

- if it is discovered that you do not meet the study requirements,
- if you become pregnant,
- if your disease gets worse,
- if you need a treatment that is not allowed in this study,
- at the discretion of the study doctor, or
- if the study is canceled.

If you are taken off the study, you will be told the reason why.

8. What are the possible disadvantages and risks of taking part?

ASTX727 (oral decitabine and cedazuridine)
No safety issues have been identified to date with ASTX727 that are inconsistent with the safety profile of its individual components. Neutropenia (low levels of a type of white blood cell called neutrophils), and thrombocytopenia (low levels of blood platelets) are known risks of one of the components of ASTX727 and as such, are potential risks of ASTX727. Based on findings from animal studies and its mechanism of action, one of the components of ASTX727 can cause fetal harm (hazard to an unborn child) when administered to a pregnant woman and as such, is a potential risk of ASTX727.

Based on clinical experience with ASTX727, the most common side effects (occurring in at least 10% of subjects) associated with ASTX727 are:

- Thrombocytopenia/platelet count decreased – low blood platelet count
- Neutropenia/neutrophil count decreased – low levels of neutrophils (a type of white blood cell) in the blood
- Anemia – low levels of red blood cells
- Febrile neutropenia – low levels of neutrophils in the blood associated with fever
- Leukopenia – low levels of leukocytes (a type of white blood cell) in the blood
- Constipation and/or abdominal pain
- Nausea, vomiting, and diarrhea – which can cause low levels of salt (sodium) in the blood
- Fatigue – extreme tiredness
- Decreased appetite and/or weight loss
- Infection in the mouth, throat, or skin
- Infection or inflammation of the lungs called pneumonia. This could lead to the lungs not functioning properly and you may experience fever, cough and/or shortness of breath
- Inflammation of the mucous membrane of the mouth which can worsen to include ulcers in the mouth. This can cause mouth pain and difficulty swallowing
- Urinary tract infection which may cause you to experience pain while urinating
- Fever with or without chills
- Bleeding from the nose, mouth, skin, urinary bladder, stomach, or may be noticed in the white part of the eye
- Swelling of tissues (also called edema) usually in face, arms or legs that could be the result of infection or low level of albumin (a protein in blood)
- Increase in liver enzymes, which can result in your eyes or skin appearing yellow, or dark urine
- Increased levels of a waste product called creatinine, which is a sign of abnormal kidney function as a result of infection
- High blood sugar (also called hyperglycemia)
- Abnormal, fast, or irregular heartbeat due to infection or low red blood cells
- Generalized aches and pains including in joint, limb and body aches

- Headache
- Skin rash
- Trouble sleeping
- Falls due to low red blood cells or a lack of oxygen, which results in dizziness
- Decrease in blood pressure due to anemia or infection

The following side effects can be life threatening and/or fatal:

- As described above, a decrease in certain blood cells may be life-threatening. It may result in severe infection, bleeding, and possibly death, even with medical care. If you experience fever or other signs and symptoms of infection or bleeding, you should contact your study doctor or study nurse right away and seek medical attention.
- Serious cases of infection in the body may result in a decrease in blood pressure, your kidneys not working adequately, or your heart suddenly stopping. This is a syndrome of events called sepsis/septic shock.
- In rare cases, bleeding in the brain has been reported.
- In rare cases, tumor lysis syndrome has been reported. This is a condition that can occur after treatment of a fast-growing cancer, especially certain leukemias and lymphomas, also called cancers of the blood. As tumor cells die, they break apart and release their contents into the blood. This causes a change in certain chemicals in the blood. This may cause damage to organs, including the kidneys, heart, and liver. This collection of side effects may include nausea with or without vomiting, lack of appetite and fatigue, dark urine, flank pain, reduced urine output, or kidney failure, seizures or hallucination in severe cases, numbness, muscle cramps and heart palpitations or irregular heart rate.

In rare cases, these reactions to ASTX727 have been reported:

- Hypersensitivity reaction related to the drug, which could include one or more of the following: rash; hives; swelling of the face, lips, tongue or throat; and difficulty swallowing or breathing.
- Sweet's syndrome (acute neutrophilic dermatosis): a skin condition that also involves the lungs and may include cough, shortness of breath, fever, and a painful rash on the arms, legs, trunk, face, or neck.

The side effects from ASTX727 are expected to be similar to those from intravenous decitabine. Therefore, there is also a rare possibility that you could experience events of differentiation syndrome or interstitial lung disease (described below). However, these events have not been reported in ASTX727 studies thus far:

- Differentiation syndrome: This is the name for a group of conditions caused by immature cells in the bone marrow or blood that upon treatment with certain medicines may cause immature cells to rapidly grow and mature. This may cause you to experience fever; cough; trouble breathing; weight gain; swelling of the arms, legs, and neck; build-up of fluid around the heart and lungs; low blood pressure; and kidney failure and could be life threatening.
- Interstitial lung disease: This is the name for a large group of diseases that inflame or scar the lungs. The inflammation and scarring make it hard to get enough oxygen. The scarring is called pulmonary fibrosis. This may cause you to experience cough, shortness of breath, tiredness, low oxygen in your blood, and generally feeling unwell. This may also include a condition called clubbing. Clubbing is changes in the areas under and around the toenails and fingernails. The nails may also show changes. This can be a serious complication requiring treatment.

You will be taking Itacitinib with ASTX727 together. These drugs have not been given together before. Therefore, you may experience side effects not listed above because they are not yet known. Taking these drugs together could also increase your risk of having the side effects listed above.

Itacitinib
Itacitinib has been administered to healthy adult subjects as well as subjects with rheumatoid arthritis, psoriasis, myelofibrosis solid tumors, B-cell malignancies, and graft-versus-host disease and has generally been well tolerated. Adverse events occurring frequently in subjects receiving itacitinib depended upon the subject's underlying disease and whether itacitinib was given alone or in combination with another therapy.

Itacitinib has been shown to affect blood cell parameters. In the INCB 39110-230 study, monotherapy itacitinib was given to 87 subjects with myelofibrosis. The most frequently reported side effects occurring in more than 25% of subjects treated at all dose levels included anemia (low red blood cell count; 39.1%), fatigue (35.6%), and low platelet count (25.3%).

Hyperlipidemia (abnormally high levels of fats in the blood) has previously been noted in subjects receiving drugs that are similar to itacitinib. In the cancer patient population, monitoring and treatment of hyperlipidemia should be tailored as appropriate based on individual subject characteristics, while exercising caution on study with cholesterol-lowering agents.

Very common (occurring in at least 10% of subjects) side effects associated with itacitinib monotherapy (single drug treatment) are:	
• Anemia – low red blood cell count • Fatigue – extreme tiredness • Thrombocytopenia – low blood platelet count • Upper respiratory tract infection – acute infections involving the nose, throat and lungs • Nausea – feelings of sickness with an urge to vomit • Diarrhea • Constipation • Cough • Peripheral edema – swelling due to fluid buildup, usually in lower limbs • Fever • Dizziness • Dyspnea – shortness of breath • Abdominal pain	• Arthralgia – joint pain • Limb pain • Rash • Contusion – bruising • Headache • Night sweats • Pruritus – itching • Back pain • Vomiting • Epistaxis – nose bleeds • Fall • Decreased appetite • Elevated blood pressure • Pneumonia • Muscle spasm
Very common (occurring in at least 10% of subjects) side effects associated with itacitinib in combination with chemotherapeutic agents are:	
• Diarrhea • Fatigue – extreme tiredness • Febrile neutropenia – low levels of neutrophils associated with fever • Decreased appetite • Dyspnea – shortness of breath • Arthralgia – joint pain • Chills	• Cough • Dizziness • Dysgeusia – distortion of the sense of taste • Headache • Hypoxia – below normal level of oxygen in the blood • Nausea

- Constipation
- Epistaxis – nose bleeds
- Muscular weakness
- Myalgia – muscle pain
- Peripheral edema – swelling due to fluid buildup, usually in lower limbs
- Blood bilirubin increased – elevated levels of a blood breakdown product
- Oral/oropharyngeal pain
- Pulmonary embolism – blocked blood vessel in the lungs
- Fever
- Upper respiratory tract infection – acute infections involving the nose, throat and lungs
- Vomiting

CT Scan Risks
Computed tomography (CT) scans send x-rays through the body at many different angles. Some people may feel "closed in" while lying in the CT scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. You will usually need to drink a liquid to help define various abdominal organs. This may cause nausea and/or vomiting. A solution with a dye may also be given by vein to make the x-ray pictures more accurate and this may cause redness, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching. Patients with poor kidney function may be ineligible for this test as determined by your study doctor. When a CT scan of the abdominal area is taken, an enema may be used to insert fluid into the rectum to better define the bowel. Your study doctor will discuss with you whether you should have a CT scan with a dye based on your health status.

Radiation Risks
If you take part in this study, you may have up to four CT procedures imaging your abdomen. These procedures expose you to radiation and are for research purposes only. The amount of radiation that you could receive is about 90% or 9/10th the amount allowed annually for a person exposed to radiation as part of their work.

Bone Marrow Biopsy or Aspirate Risks
Your study doctor will explain the risks associated with collecting the bone marrow biopsy or aspiration. Having a biopsy or aspiration performed may cause some pain, bruising, redness, inflammation, bleeding, low blood pressure, swelling and/or infection at the site of the biopsy or aspiration. An allergic reaction to the anesthetic may occur. A scar may form at the aspiration site. If lidocaine is used as a numbing drug, it may burn or cause a rash, redness, or soreness where you get the shot. There is a risk that lidocaine may cause problems with heart rhythm.

Blood Draw Risks
Blood samples will be taken during the study and at certain visits. Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely, some people faint. The study doctor may put some cream (called EMLA) on your skin to numb the area so you will not feel the needle stick as much. The numbing cream may make your skin, or the area have a change in skin color, but this is rare.

ECG Risks
An electrocardiogram (ECG) is a simple and painless test that detects and records the electrical activity of your heart. Soft adhesive patches (the size of a quarter) will be attached to the skin of the chest, arms, and legs. You will be requested to lie still for a few minutes while a machine records the electrical signals. Rarely, localized rash or skin irritation may occur where the adhesive patches are placed. These reactions are typically temporary.

Women of Childbearing Potential

If you are pregnant (or plan to become pregnant) or if you are breast feeding, you cannot take part in this study. The study drugs could have a bad effect on you or your child. If you are a woman who is able to become pregnant, you must agree to use a highly effective method of birth control while on treatment and for four months after your last dose of study drug to prevent exposing your baby to a possibly dangerous unknown risk.

Highly effective methods of birth control include:

- True abstinence (not periodic abstinence or withdrawal)
- Sterilization (surgical bilateral oophorectomy with or without hysterectomy, tubal ligation, vasectomized partner at least six weeks before starting treatment)
- Use of a combination of two of the following:
  a) Barrier methods with spermicide
    - condom (male or female)
    - occlusive cap (diaphragm or cervical/vault caps/shield)
    - use of two barrier methods is acceptable (i.e., male condom + diaphragm or equivalent)
  a) Placement of an intrauterine device (IUD) or intrauterine system (IUS).
  b) Hormonal implants or combined oral contraceptives

The following birth control methods are **not acceptable:**

- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal

To make sure you are not pregnant, you must agree to have a pregnancy test done within 3 days before starting the first dose of study drug. A repeat pregnancy test must be done if you miss any periods or if your menstrual cycle becomes irregular.

You must accept the risk that pregnancy might still occur despite the responsible use of a reliable method of birth control.

Tell the study doctor as soon as possible if you fail to use your birth control method properly or if you become pregnant. In both cases, you can no longer take part in the study. If you become pregnant, the study doctor or study staff will tell you about the possible risks to your unborn child and the options available to you. You will also be contacted to learn about the outcome of your pregnancy.

Men Only
If you are a male who can father children, the effect of the study drug on your sperm is unknown. You must use a condom with spermicide during the study and for at least four months after the last dose of study drugs. This is done to prevent pregnancy in your partner, which could expose the unborn child to an unknown risk. You must not donate sperm while on treatment and for at least four months after your last doses of study drug.

As the risk to your partner and the baby are unknown, if your partner becomes pregnant, she will be asked to sign a consent form to allow medical follow-up concerning the outcome of her pregnancy. A copy of this form is available for your review. Dr. Michael Savona or research staff will follow-up with the obstetrician regarding regularly scheduled visits.

Risks that are not known:
Because this treatment is investigational, meaning not approved by the Food and Drug Administration (FDA), there may be risks that we do not know about at this time.

9. Are there benefits to taking part in the study?

The benefits to science and humankind that might result from this study:

a) The information collected during this study will help the doctors and researchers to learn more about the study treatment that may benefit you and other people with your disease. However, there is no guarantee that this will happen.

The benefits you might get from being in this study:

b) If you agree to take part in this study, there may or may not be direct medical benefit to you. Your condition may even get worse during the study.

10. Compensation

You will not receive any payment for taking part in this study.

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11. What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment/getting palliative care

Discuss your choices with your doctor before you decide if you will take part in this study.

12. What if new information becomes available?

Sometimes, during the course of a research project, new information becomes available on the drug that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to stay on the study. If you decide to stop, you should tell your study doctor and he or she will arrange for your care to continue. If you decide to stay on the study, you may be asked to sign an updated informed consent form.

On receiving new information, your study doctor might think it is in your best interests to stop your participation in the study. If so, he or she will explain the reasons for his or her decision and arrange for your care to continue.

13. Will my medical information be kept confidential?

The Sponsor, Dr. Michael Savona and/ or Vanderbilt, and/or its representative (Theradex Oncology) may share your information, without identifiers, to others (including Astex Pharmaceuticals, Inc. and Incyte Corporation) or use it for other research projects not listed in this form. Theradex Oncology, Vanderbilt, Dr. Michael Savona and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

Every effort will be made to keep your personal health information (PHI) confidential. Your PHI includes your name and address, medical records, and information collected during the study. Your PHI will be kept confidential as much as possible as required by law.

People involved with the study, including doctors, nurses, and researchers, will see the records that have your name and address so that they can follow the progress of the study. Information in these records will be shared with people involved with the study, but your name and PHI will never be used. No names or other identification will be in any study documents. Also, your records may be seen by people from regulatory authorities, Sponsor representatives or designees or auditors. These people may also review your entire medical record. If the results of this study are published, you will not be identified by name.

If you leave the study or after your participation has been stopped for any other reason, any information collected while you were in the study will be kept and may be included in the final results of the study.

14. Privacy

Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

15. What will happen to the results of this study?

When the study has finished and all the data have been collected, a report will be written and the results will be published in a medical or scientific journal, and/or presented at scientific meetings, and used for further research purposes. The results will be published in anonymous form so that the study participants cannot be identified. The location of the publication(s) will not be known until nearer the time. If you wish, you may contact your study doctor to receive a copy of the results.

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.

Clinical Trials Reporting Program.
Vanderbilt's NCI-Designated Cancer Center or the Sponsor registers National Cancer Institute (NCI)-supported clinical trials with NCI though their Clinical Trials Reporting Program (CTRP) to provide study related information. The data provided will include the following identifiable information that may identify you: birth month/year and five-digit zip code. NCI uses the data to manage and enhance the nation's investment in cancer research.

A summary of the results may also be published at conferences or in journals. If the results of the study are presented to the public, you will not be named. Some authorities may ask that Sponsor disclose study data for transparency reasons. However, the data shared will not identify you.

16. Consent to use/disclose protected health information

What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both the Sponsor and others) may release

your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use, or share the information?
The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other Sponsor representatives, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of the Sponsor. This may include the Sponsor's agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Is my health information protected after it has been given to others?
All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at VUMC, are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies who might have access to your information may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission. Your personal information may be disclosed if required by law.

Do you have to allow this Authorization?
You do not have to allow this Authorization, but if you do not, you may not join the study. Signing this consent form indicates that you are allowing this authorization.

How long will your information be used or shared?
Your consent for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this consent at any time. If you cancel, you must contact your study doctor in writing to let them know by using the contact information provided in this consent form. Deciding to not be part of the study will not change your regular medical care in any way. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your consent. Unless told otherwise, your consent to use or share your PHI does not expire. You understand that the revocation will not apply to your insurance company when the law provides your insurance company with the right to contest a claim under your policy. If you change your mind, we ask that you contact Dr. Michael Savona in writing and let them know that you withdraw your consent. Their mailing address is:

2220 Pierce Avenue

777 Preston Research Building
Nashville, TN 37232

Consent for sample and data storage and future research
You will have blood bone marrow and blood cells taken as a part of this research study. What we learn about you from these samples will not be put in your health record. Your test results will not be shared with you or your study doctor. No one else (like a relative, boss, or insurance company) will be given your test results.

Bone marrow biopsy or aspirate
You will have a blood and bone marrow samples taken as part of the study for exploratory analysis, which may include genome sequencing. This means we will map part of your genetic code. The results will be used to compare your 'normal' DNA sequences with those of your tumor samples. The results will be reported independently of this study. You will not be named in any report.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only the study doctor and his team will have access to your name.

Your samples will be kept for up to 10 years for future research. The samples will be destroyed when they are no longer needed. Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Sponsor, and/or others. If this happens, there are no plans to provide money to you.

Your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your sample may be used to develop new drugs or other products for commercial purposes. If these products make money, there are no plans to share the money with you.

At any time, you may ask to have your samples destroyed. You should contact your study doctor at 2220 Pierce Ave., 777 Preston Research Building, Nashville, TN 37232, or at 615-322-5000 or (877) 936-8422 (24 hours) to have your samples destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your samples. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

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

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at:
http://cancer.gov/clinicaltrials/understanding/insurance-coverage.

You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

18. Who is organizing and funding this study?

This study is being Sponsored by Vanderbilt University Medical Center and Theradex Oncology. The Vanderbilt University Medical Center address is 1211 Medical Center Drive, Nashville, TN 37232. Theradex Oncology is located at 4365 Route 1 South, Suite 101, Princeton, NJ 08540. Astex Pharmaceuticals, Inc. is providing the study drug ASTX727, and Incyte Corporation is providing the other study drug, Itacitinib. The doctors conducting the study are not being paid, but a payment will be made to the hospital to cover the cost of the study tests and procedures. Your study doctor will tell you if he or she has any financial or other ties with Vanderbilt University Medical Center.

19. What happens if I am injured because I took part in this study?
If it is determined by Vanderbilt and the Investigator with Sponsor input that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury.

There are no plans for Vanderbilt or the Sponsor to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt or the Sponsor to give you money for the injury.

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

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this 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 regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our clinic.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

21. Who has approved the study?

The study has been reviewed and approved by a group of people called an Institutional Review Board (IRB). An IRB is a group of people who perform independent review of research as required by regulations. For this study, the Vanderbilt Institutional Review Board is responsible.

22. Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact Dr. Michael Savona at 615-322-5000 or (877) 936-8422 (24 hours). If you think you have been injured as a result of taking part in the study, contact Dr. Michael Savona at 615-322-5000 or (877) 936-8422 (24 hours).

If you have any questions regarding your rights or if you experience a research related injury, you may contact the Vanderbilt Institutional Review Board at (615) 322-2918 or toll free at (866) 224-8273.

If at any time during this study you feel that you have not been informed enough about your privacy rights about your health information, or you feel that the privacy of your health information was not protected, you may contact the Vanderbilt Institutional Review Board at (615) 322-2918 or toll free at (866) 224-8273.

CONSENT FORM FOR CLINICAL RESEARCH

The ABNL-MARRO 001 Study: A Phase 1/2 Study of Active Myeloid Target Compound Combinations in MDS/MPN Overlap Syndromes

Patient Statement

I, the undersigned, have been told about this research study. I have been informed about the procedures to be followed, the possible risks and the benefits that I may experience as a result of my taking part. I have read the description of this research (or had it translated into a language I understand) and had the opportunity to ask questions. I understand that my participation is voluntary and that I may withdraw from the study at any time without penalty or loss of any benefits I may otherwise be entitled to. I agree to take part in this research study.

I understand that any of my medical records may be inspected by Vanderbilt University Medical Center and their representatives, or by people from the Vanderbilt Institutional Review Board or by Food and Drug Administration (FDA) regulatory authorities to check that the study is being carried out correctly.

I consent to the blood and bone marrow sample procedures required in this study and for my blood and bone marrow samples to be stored and used for future research.

I may contact Dr. Michael Savona at any time with questions about this study.

I have been given a copy of the patient information sheet and consent form.

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person Conducting Informed Consent Discussion	Date	Signature
_____	_____	_____
Name of Witness *(if applicable)*	Date	Signature