ADULT CONSENT - CLINICAL BIOMEDICAL

Title of this Research Study
A Phase II Study of the Impact of Clinicogenetic Risk-Stratified Management on Outcomes of Acute Myeloid Leukemia Older Patients

Invitation
You are invited to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- "The Rights of Research Subjects"

Why are you being asked to be in this research study?
You are being asked to be in this study because you are at least 60 years old and have a diagnosis of acute myeloid leukemia (AML).

We will enroll 75 patients in this study over a 4-5 year period.

What is the reason for doing this research study?
This research is trying to determine if treatment of acute myelogeneous leukemia will improve the chance of a better outcome if the dose and drugs used are based on specific genetic characteristics of the leukemia and the subject's general health.

What will be done during this research study?
Before you enter the study
As a part of the routine care, you will undergo the following tests to find out if you can participate in the study:

- A physical exam, including your medical history, height, weight, body mass index (BMI) and vital signs.
- A bone marrow biopsy with aspirate and tests to determine what the specific genetic abnormalities are in your leukemia.
- A MUGA or echocardiogram or stress echocardiogram (these tests tell how well your heart is functioning).
- Routine laboratory test of your blood

.At baseline after you enter the study

- A thorough assessment of your health, also known as geriatric assessment. This includes additional physical assessment and five questionnaires
- Answer one questionnaire that will be used to determine your quality of life

status.

Once the assessments are completed, either a low-intensity or intensive chemotherapy will be selected for you. The therapy will be determined by your health assessment results and the genetic abnormalities in your disease.

All the therapies used in this study are considered standard of care for patients with AML. Your study doctor will talk to you about the treatment plan that will be best for you.

Treatment schedule for Intensive Induction (Initial Chemotherapy) and Consolidation Therapy (treatment given after remission has been achieved)

Cytarabine and idarubicin is the preferred intensive induction therapy for this study. Some patients may also be given CPX 351, if appropriate for their diagnosis. Intermediate-dose cytarabine is the standard of care consolidation therapy for patients receiving intensive induction therapy.

A treatment cycle is round of chemotherapy followed by a recovery period. The duration of each cycle of consolidation therapy will be approximately 4 weeks, but may be prolonged by another 2 weeks based on your recovery from any side effects or your blood count recovery.

Intensive induction therapy with cytarabine (100-200 mg/m^2 dose) and idarubicin (12 mg/m^2 dose) or CPX-351 (dose of daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) is given for one cycle. If you do not respond, you will receive salvage (second line) therapy at the discretion of your treating doctor.

Once you go into remission, consolidation therapy will be started. Consolidation therapy will be 2 -4 cycles of cytarabine (1000-1500 mg/m^2 dose) or CPX 351 (dose of daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2). If you are able to proceed to an allogeneic transplant, or are not able to tolerate further treatment, your study doctor may decide to stop the consolidation therapy.

Treatment Schedule for Low-Intensity Induction and Consolidation therapy

The duration of each cycle of venetoclax and azacitidine or decitabine therapy will be approximately 4 weeks but may be prolonged by another 2 weeks based on your recovery from any side effects or your blood count recovery.

The total therapy with induction and consolidation courses of low-intensity chemotherapy will be continued for 3 or more cycles.

If you are able to proceed to an allogeneic transplant, or if you are not able to tolerate further treatment, your study doctor may stop chemotherapy.

At about day 10 you will be asked to complete two questionnaires. One questionnaire will be used to determine your quality of life status.

The follow up assessments are discussed below. These assessments are performed when you are expected to return for your routine care.

About 4 weeks after initiation of chemotherapy

- A bone marrow biopsy and aspirate (if count recovery and no evidence of disease on blood tests).
- Routine laboratory test of your blood, which include a Complete Blood Count (CBC) and Comprehensive Metabolic Panel (CMET)
- A thorough assessment of your health, also known as geriatric assessment. This includes physical assessment and four questionnaires.
- Answer one questionnaire that will be used to determine your quality of life status.

About 8 weeks after initiation of chemotherapy

- A bone marrow biopsy and aspirate (if complete remission is not documented previously).
- Routine laboratory test of your blood, which include a Complete Blood Count (CBC) and Comprehensive Metabolic Panel (CMET)

About 90 days after initiation of chemotherapy

- A bone marrow biopsy and aspirate (if complete remission is not documented previously).
- Routine laboratory test of your blood, which include a Complete Blood Count (CBC) and Comprehensive Metabolic Panel (CMET)
- A thorough assessment of your health, also known as geriatric assessment. This includes physical assessment and four questionnaires.
- Answer one questionnaire that will be used to determine your quality of life status.

Post-trial Assessments

If you go off study treatment at any time during the trial, you will be followed for side

effects for 30 days after the last day of treatment or until other disease-related treatment begins. You can refuse any of these additional assessments.

Follow up

If at anytime you go off study treatment, we will ask you to continue with study procedures, assessments and questionnaires. You can refuse to complete these procedures, assessments and questionnaires.

After the completion of chemotherapy, we will contact you for follow up about every 3 months for up to 2 years to keep track of how you are doing and if your disease has come back. Keeping in touch with you and checking your health helps us look at the long-term effects of the research study.

What are the possible risks of being in this research study?

The use of cytotoxic chemotherapy is associated with numerous potential risks. It is believed the treatment options outlined in the study will not pose significant additional risks compared to conventional treatment that might consist of similar chemotherapy drugs given alone or in combination.

Possible Side Effects of Cytarabine

- Cardiovascular
  - chest pain caused by lack of oxygen to the heart (Angina pectoris)
  - chest pain
  - blockage of blood flow in the liver (hepatic veno-occlusive disease - also called hepatic sinusoidal obstruction syndrome)
  - inflammation of your veins (local thrombophlebitis)
  - inflammation of the tissue surrounding the heart (pericarditis)
- Central nervous system
  - inflammation of the tissue surrounding the brain (aseptic meningitis)
  - localized brain dysfunction (cerebral dysfunction)
  - dizziness
  - headache
  - inflammation of the nerves (neuritis)
  - toxicity to the nervous system
  - paralysis (IV combination therapy)
  - reversible posterior leukoencephalopathy syndrome (a syndrome characterized by headache, confusion, seizures and visual loss)
- Dermatologic
  - sudden rash with swelling and redness of the skin (acute generalized exanthematous pustulosis)

- hair loss (alopecia)
- skin sores (dermal ulcer)
- red or brown spots on the skin (ephelis)
- itching (pruritus)
- skin rash
- urticaria (hives)

- Endocrine & metabolic
  - excessive uric acid (hyperuricemia)
- Gastrointestinal
  - Abdominal pain
  - anal fissure
  - anal inflammation
  - loss of appetite (anorexia)
  - diarrhea
  - esophageal ulcer
  - inflammation of the esophagus (esophagitis)
  - increased serum amylase (a digestive enzyme)
  - increased serum lipase (a digestive enzyme)
  - tissue destruction in the intestines (intestinal necrosis)
  - inflammation of the tissue lining the digestive tract (mucositis)
  - nausea
  - inflammation of the pancreas
  - sore throat
  - enlarged colon (toxic megacolon)
  - vomiting
- Genitourinary
  - Urinary retention
- Hematologic & oncologic
  - Anemia
  - bone marrow depression
  - hemorrhage
  - reduced number of white blood cells (leukopenia)
  - enlarged red blood cells that do not function correctly (megaloblastosis)
  - decreased neutrophil cells in the blood (neutropenia)
- Hepatic
  - liver failure (hepatic insufficiency)
  - increased liver enzymes (increased serum transaminases)
  - jaundice
- Hypersensitivity

- swelling of tissue from an allergic reaction (allergic edema)
- severe allergic reaction (anaphylaxis)

- Infection
  - infection of the blood (sepsis)
- Neuromuscular & skeletal
  - destruction of muscle tissue (rhabdomyolysis)
- Ophthalmic
  - inflammation of the eye (conjunctivitis)
- Renal
  - kidney failure (renal insufficiency)
- Respiratory
  - acute respiratory distress
  - shortness of breath (dyspnea)
  - lung tissue inflammation/destruction (interstitial pneumonitis)
- Miscellaneous
  - Drug toxicity (cytarabine syndrome; a syndrome characterized by chest pain, eye infection, fever, raised rash, malaise, muscle pain, bone pain)
  - fever
- Hypersensitivity
  - allergic reaction resulting in heart failure has been reported (rare)
  - tumor lysis syndrome (toxins released by the death of cancer cells) and subsequent high uric acid levels may occur.

Possible Side Effects of High-dose Cytarabine

- Cardiovascular
  - enlarged heart (cardiomegaly)
  - heart muscle weakening (cardiomyopathy - in combination with cyclophosphamide)
- Central nervous system
  - toxicity to the nervous system (patients with renal impairment)
  - coma
  - drowsiness
  - brain toxicity (neurocerebellar toxicity)
  - numbness of the hands and feet (peripheral neuropathy - motor and sensory)
  - personality changes
- Dermatologic
  - complete hair loss (alopecia)
  - peeling of the skin (desquamation)

- skin rash (severe)

- Gastrointestinal
  - Gastrointestinal ulcer
  - death of intestinal tissue (necrotizing enterocolitis)
  - inflammation of the pancreas (pancreatitis)
  - inflammation of the tissue surrounding the abdominal cavity (peritonitis)
  - pneumatosis cystoides intestinalis (a bowel disease)
- Hepatic
  - liver infection (hepatic abscess)
  - liver injury (hepatic injury)
  - increased bilirubin in the blood (hyperbilirubinemia)
- Infection
  - blood infection (sepsis)
- Ophthalmic
  - damage to eye tissue (corneal toxicity)
  - severe eye infection (hemorrhagic conjunctivitis)
- Respiratory
  - difficulty breathing (acute respiratory distress)
  - fluid in the lungs (pulmonary edema - severe shortness of breath with a rapid decrease in blood oxygen, leading to respiratory failure; may be fatal)

Possible Side Effects of Idarubicin

Frequency >10%

- Cardiovascular
  - Cardiac failure (dose-related)
  - abnormal heart rhythms (ECG abnormalities)
- Central nervous system
  - Headache
- Dermatologic
  - hair loss (alopecia)
  - skin rash
  - hives - welts with intense itching (urticaria)
- Gastrointestinal
  - Vomiting
  - gastrointestinal hemorrhage
  - diarrhea
  - inflammation of the mouth (stomatitis)

- nausea
- Genitourinary
  - Urine discoloration (darker yellow)
- Hematologic & oncologic
  - Anemia
  - bone marrow suppression; decreased white blood cells (primarily leukopenia)
  - decreased platelets (thrombocytopenia)
- Hepatic
  - Increased blood bilirubin
  - increased liver enzymes (increased serum transaminases)
- Miscellaneous
  - inflammation of the skin that previously received radiation (radiation recall phenomenon)

Frequency 1% to 10%

- Central nervous system
  - numbness of the hands and feet (peripheral neuropathy)
  - seizure

Frequency < 1% (Limited to important or life-threatening)

- enlarged heart (cardiomyopathy)
- excessive uric acid (hyperuricemia)
- inflammation of the heart muscle (myocarditis)
- inflammation of the large intestine (typhlitis - neutropenic)
- miscellaneous toxicities: vesicant; may cause severe local tissue damage and tissue death.

Possible Side Effects of CPX-351, a liposomal preparation of daunorubicin and cytarabine

Frequency >10%

- Cardiovascular:
  - Edema
  - Altered heart beat (cardiac arrhythmia)
  - Toxic effect on the heart (cardiotoxicity)
  - Low blood pressure (hypotension)
  - High blood pressure (hypertension)
  - chest pain
- Central nervous system:

- Headache
- fatigue
- sleep disorder
- chills
- dizziness
- confused thinking and attention with altered speech and hallucinations (delirium)
- anxiety

- Dermatologic:
  - Skin rash
  - Itching (pruritus)
- Endocrine & metabolic:
  - Low levels of blood sodium (hyponatremia)
- Gastrointestinal:
  - Diarrhea
  - nausea
  - inflammation of the colon (colitis)
  - inflammation of the membranes lining the gastrointestinal tract (mucositis)
  - constipation
  - abdominal pain
  - decreased appetite
  - vomiting
  - hemorrhoids
- Hematologic & oncologic:
  - Low red blood cell counts (anemia)
  - Low white blood cell counts (neutropenia)
  - low platelet counts (thrombocytopenia)
  - bleeding (hemorrhage)
  - fever due to low white blood cell counts (febrile neutropenia)
  - red spots on skin due to bleeding (petechia)
- Hypersensitivity:
  - Transfusion reaction
- Infection:
  - Bacteremia or fungal infections, or sepsis
  - At the site of the injection site reaction
- Musculoskeletal pain
- Visual impairment
- Renal insufficiency
- Respiratory:

- Cough
- difficult breathing (dyspnea)
- pneumonia
- lack of oxygen (hypoxia)
- upper respiratory tract infection
- fluid surrounding the lungs (pleural effusion)

- Miscellaneous: Fever

Frequency 1% to 10%

- Hallucination
- Endocrine & metabolic:
  - Low blood potassium levels (hypokalemia)
  - Low blood albumin (hypoalbuminemia)
  - abnormal liver enzyme (alanine aminotransferase)
- Indigestion (dyspepsia)
- High levels of blood bilirubin (Hyperbilirubinemia)
- Ophthalmic:
  - Eye infection (conjunctivitis)
  - dry eye syndrome
  - eye irritation
  - eye pain
  - injected sclera
  - excess blood in the eye (ocular hyperemia)
  - swelling of the eye orbital (periorbital edema)
  - swelling of eye
- Deafness
- Inflammation of the lungs (pneumonitis)

Possible Side Effects of Decitabine

Frequency >10%

- Cardiovascular
  - swelling of extremities (peripheral edema)
  - swelling (edema)
  - heart murmur
  - low blood pressure (hypotension)
- Central nervous system
  - fatigue
  - headache
  - insomnia

- shivering (rigors)
- dizziness
- chills
- pain
- confusion
- lethargy
- reduced sense of touch (hypoesthesia)
- anxiety

- Dermatologic
  - Pallor
  - skin rash, redness, skin infection, itching
- Endocrine & metabolic
  - high blood sugar (hyperglycemia)
  - decreased albumin (hypoalbuminemia)
  - decreased magnesium (hypomagnesemia)
  - decreased potassium (hypokalemia)
  - decreased sodium (hyponatremia)
  - increased potassium (hyperkalemia)
- Gastrointestinal
  - Nausea
  - constipation
  - diarrhea
  - vomiting
  - loss of appetite (anorexia)
  - decreased appetite
  - abdominal pain
  - inflammation of the mouth (stomatitis)
  - indigestion (dyspepsia)
- Hematologic & oncologic
  - decreased neutrophil cells (neutropenia)
  - decreased platelets (thrombocytopenia)
  - anemia
  - red spots on the skin (petechia)
  - fever with low white blood cell counts (febrile neutropenia)
  - decreased white blood cell counts (leukopenia)
  - bruise
  - red spots in the mouth (oral mucosal petechiae)
  - enlarged lymph nodes (lymphadenopathy)
- Hepatic
  - increased bilirubin in the blood (hyperbilirubinemia)

- increased liver enzyme (increased serum alkaline phosphatase)

- Local
  - localized tenderness
- Neuromuscular & skeletal
  - joint pain (arthralgia)
  - limb pain
  - back pain
  - weakness
- Respiratory
  - cough
  - shortness of breath (dyspnea)
  - pneumonia
  - inflammation of the throat (pharyngitis)
  - abnormal breath sounds (rales)
  - nose bleeds (epistaxis)
- Miscellaneous
  - Fever

Frequency 5% to 10%:

- Cardiovascular
  - increased heart rate (tachycardia)
  - chest wall pain
  - chest pain
  - chest discomfort
  - facial swelling
  - high blood pressure (hypertension)
  - cardiac failure
- Central nervous system
  - depression
  - falling
  - feeling of discomfort (malaise)
  - mouth pain
- Dermatologic
  - hair loss (alopecia)
  - skin dryness (xeroderma)
  - rash (urticaria)
  - catheter site redness
  - night sweats
- Endocrine & metabolic
  - increased uric acid (hyperuricemia)

- weight loss
- increased lactate dehydrogenase (a blood enzyme)
- dehydration
- decreased chloride (hypochloremia)
- increased blood alkalinity (increased serum bicarbonate)
- increased blood acidity (decreased serum bicarbonate)
- decreased protein (hypoproteinemia)

- Gastrointestinal
  - inflammation of the mouth (mucosal inflammation)
  - bleeding gums (gingival hemorrhage)
  - hemorrhoids
  - loose stools
  - tongue ulcer
  - fungal infection of the mouth (oral candidiasis)
  - toothache
  - dysphagia (difficulty swallowing)
  - abdominal distention
  - heartburn (gastroesophageal reflux disease)
  - pain in the tongue (glossalgia)
  - mouth sores (oral mucosa ulcer)
- Genitourinary
  - urinary tract infection
  - painful or difficult urination (dysuria)
- Hematologic & oncologic
  - bruising (hematoma)
  - decreased blood cell production (pancytopenia)
  - excessive platelets (thrombocythemia)
- Hepatic
  - abdominal fluid (ascites)
  - increased liver enzyme (increased serum AST)
  - decreased serum bilirubin
- Hypersensitivity
  - Transfusion reaction
- Infection
  - yeast infection (candidiasis)
  - bacteremia
  - staphylococcal infection
  - tooth abscess
- Local
  - catheter infection

- catheter pain
- swelling at injection site

- Neuromuscular & skeletal
  - muscle pain (myalgia)
  - muscle spasm
  - bone pain (ostealgia)
  - musculoskeletal discomfort
  - musculoskeletal pain
  - cracking sounds in the joints (crepitations)
- Ophthalmic
  - Blurred vision
- Otic
  - earache (otalgia)
- Renal
  - increased urine (polyuria)
- Respiratory
  - decreased blood oxygen (hypoxia)
  - upper respiratory tract infection
  - abnormal breath sounds
  - pain in the upper abdominal area (pharyngolaryngeal pain)
  - pulmonary edema
  - sinusitis
  - fluid surrounding the lungs (pleural effusion)
  - post nasal drip
  - sinus congestion

Frequency < 5% (Limited to important or life-threatening)

- abscess in the area surrounding the intestines (abscess-peridiverticular)
- acute cardiorespiratory failure
- severe allergic reaction (anaphylaxis)
- irregular heart rate (atrial fibrillation)
- weakening of the heart muscles (cardiomyopathy)
- catheter site hemorrhage
- inflammation of the gall bladder (cholecystitis)
- fungal infection
- gastrointestinal hemorrhage
- pain in the gums (gingival pain)
- coughing up blood (hemoptysis)
- hypersensitivity reaction
- intracranial hemorrhage

- mental status change
- heart attack (myocardial infarction)
- a type of bacterial infection (mycobacterium avium complex)
- abnormal substance in the lungs (pseudomonal lung infection)
- a type of fungal infection in the lungs (pulmonary aspergillosis)
- blood clots in the lungs (pulmonary embolism)
- abnormal substances in the lungs (pulmonary infiltrates)
- pulmonary mass
- renal failure
- blood infection (sepsis)
- enlarged spleen (splenomegaly)
- abnormally fast heart rate (supraventricular tachycardia)
- a skin disease with painful skin sores (Sweets syndrome-acute febrile neutrophilic dermatosis)
- blood leaking into the urine (urethral bleeding)

Possible Side Effects of Azacitidine

Frequency >10%

Cardiovascular:

- Swelling in lower limbs (peripheral edema)
- chest pain

Central nervous system:

- Fatigue
- Chills with shivering and sweating (rigors)
- headache
- dizziness
- anxiety
- depression
- generally feeling unwell (malaise)
- pain
- inability to sleep (insomnia)

Dermatologic:

- Redness of the skin (erythema)
- Pale skin appearance (pallor)
- skin lesion
- skin rash
- very itchy skin (pruritus)
- sweating (diaphoresis)

Endocrine & metabolic:

- Weight loss
- pitting edema
- hypokalemia

Gastrointestinal:

- Nausea
- vomiting
- constipation
- diarrhea
- lack of appetite (anorexia)
- abdominal pain
- abdominal tenderness

Hematologic & oncologic:

- low platelet count (thrombocytopenia)
- anemia
- low neutrophil counts (neutropenia)
- low white blood cell count (leukopenia)
- bruising
- red spots on the skin (petechia)
- fever with low neutrophil count (febrile neutropenia)
- low blood counts (bone marrow depression)

Local:

- Injection site reactions
    - redness of the skin
    - pain
    - bruising

Neuromuscular & skeletal:

- Weakness
- Joint pain (arthralgia)
- limb pain
- back pain
- muscle pain (myalgia)

Respiratory:

- Cough
- difficult breathing (dyspnea)
- inflammation of the pharynx (pharyngitis)
- nose bleed (epistaxis)
- inflammation of the nose and throat (nasopharyngitis)
- upper respiratory infection
- pneumonia
- rales

Miscellaneous:
- Fever

Frequency 5% to 10%

Cardiovascular:
- Heart murmur
- Abnormal rapid heart rate (tachycardia)
- High blood pressure (hypertension)
- Low blood pressure (hypotension)
- A fall in blood pressure, causing loss of consciousness (syncope)
- chest wall pain

Central nervous system:
- lack of energy (lethargy)
- numbness (hypoesthesia)
- postoperative pain

Dermatologic:
- Night sweats
- Inflammation of the tissue below the skin (cellulitis)
- rash at injection site
- rash with red round welts (urticaria)
- skin nodules
- extreme dryness of the skin (xeroderma)

Gastrointestinal:
- bleeding gums (gingival hemorrhage)
- inflammation of the mouth (stomatitis)
- hemorrhoids
- indigestion (dyspepsia)
- abdominal distention
- loose stools
- unable to speak clearly (dysphagia)
- tongue ulcer

Genitourinary:
- Urinary tract infection
- Difficulty with urination (dysuria)
- Blood in the urine (hematuria)

Hematologic & oncologic:
- Disease effecting the lymph nodes (Lymphadenopathy)
- Clotted blood causing swelling within the tissue (hematoma)
- Bleeding of the mouth (oral mucosal petechiae)

- post-procedural hemorrhage
- oral bleeding

Other:

- Transfusion reaction
- Herpes simplex infection
- Lymphadenopathy
- night sweats
- Itching at injection site
- hematoma at injection site
- hardening (induration) at injection site
- reaction or swelling at injection site (granuloma)
- skin discoloration at injection site
- swelling at injection site
- mouth bleeding

Neuromuscular & skeletal:

- Muscle cramps

Respiratory:

- Runny nose (Rhinorrhea)
- wheezing
- abnormal breath sounds
- nasal congestion
- throat (pharyngolaryngeal) pain
- fluid buildup outside of lungs (pleural effusion)
- post nasal drip
- nose inflammation (rhinitis)
- whistling sound heard with breathing (rhonchi)
- collapsed lung (atelectasis)
- inflammation of sinuses (sinusitis)

Frequency < 5%

- Infection leading to pus pocket (abscess)
- bone pain
- Serious allergic reaction (anaphylactic shock)
- Problem with heart rhythm (atrial fibrillation)
- Kidney dysfunction (azotemia)
- Changes in blood salt levels including increase in uric acid (tumor lysis syndrome)
- bacterial infection
- serious infection of skin and soft tissue (necrotizing fasciitis or pyoderma gangrenosum)

- blood stream infection (sepsis or septic shock)
- lung infection (pneumonia) or inflammation (pneumonitis or interstitial pulmonary disease)
- fungal or other infection (blastomycosis toxoplamosis)
- low blood count (bone marrow failure or pancytopenia)
- heart dysfunction (cardiac failure)
- bleeding, including bleeding in the brain (cerebral hemorrhage) or gut (gastrointestinal hemorrhage)
- Coughing up blood (hemoptysis)
- infection of gall bladder (cholecystitis) or bowel (diverticulitis)
- liver damage leading to coma (hepatic coma)
- problem with blood pressure (orthostatic hypotension)
- serious problem with breathing (respiratory distress)
- abnormal shaking (seizure)
- skin reaction (Sweet's syndrome)
- skin damage (tissue necrosis) at injection site

Possible Side Effects of Venetoclax

Frequency generally >10%

- Blood and lymphatic system disorders: low platelet, white blood cell, lymphocytes or neutrophil counts, fever with low neutrophil counts, anemia, low red blood, white blood and platelet cells in the blood
- Gastrointestinal disorders: Nausea, Diarrhea, Constipation, Vomiting, Abdominal pain, decreased appetite, inflammation of the mouth, inflammation of the anus and rectum
- General disorders and administration site conditions: Swelling in lower limbs, fatigue, fever, physical wasting and malnutrition
- Multiple organ dysfunction syndrome, respiratory failure
- Infections and infestations: Pneumonia, serious blood infection (Sepsis), Urinary tract infection, inflammation of the tissue below the skin, localized infection, device related infection, upper respiratory tract infection, lower respiratory tract infection, candida infection, bacteremia, mucosal infection
- Musculoskeletal and connective tissue disorders: Back pain, muscle pain or musculoskeletal pain, arthralgia
- Nervous system disorders: Dizziness
- Skin and subcutaneous tissue disorders: Rash
- Respiratory, thoracic and mediastinal disorders: Cough, lack of oxygen, oropharyngeal pain, difficulty breathing
- Other: bleeding, gastrointestinal bleeding, low blood pressure, high blood pressure, headache, itchy skin

- Laboratory abnormalities such as; high - blood sugar, phosphorus, bilirubin, potassium, low - blood calcium, albumin, potassium, sodium, phosphorus, magnesium, Blood creatinine increased, blood bicarbonate decreased, Increased serum aspartate aminotransferase or alanine aminotransferase
- Tumor lysis syndrome including excess uric acid in the blood

Blood tests

For most people, needle punctures for blood tests do not cause any serious problems. However, they may cause fainting, bleeding, bruising, discomfort, dizziness, infections and/or pain at the injection site.

Bone marrow aspirate and/or biopsy

Risks associated with the procedure include pain, discomfort, soreness, redness, swelling, bleeding (may be excessive), bruising, and/or drainage (such as pus) at the needle site, bleeding, infection, fever, allergic reaction to the medication used to numb the skin over the biopsy site.

Risks associated with questionnaires

Patients may experience some psychological discomfort as a result of being interviewed about their health status.

Loss of confidentiality

It is possible there could be accidental release of confidential information. Every effort will be taken to make sure the patient's information remains private.

Other risks

It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before.

What are the possible benefits to you?

It is hoped that the use of risk-stratified therapy allocation may result in lower rates of toxicities from chemotherapy and early mortality rate. You may not get any benefit from being in this research study.

What are the possible benefits to other people?

Information obtained from this study may help future cancer patients by contributing to the knowledge of whether the proposed risk-stratified therapy allocation offers potential advantages over other strategies currently available.

What are the alternatives to being in this research study?
Before you decide whether or not to be in this study, your study doctor will discuss the other options that are available to you. Instead of being in this study, you could:

- Elect to receive standard therapy, which may include similar or other chemotherapy drugs given alone or in combination.
- Take part in a different research study, if available.
- Get no treatment.
- Get comfort care, also called palliative care, which helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer without treating the cancer directly.

What will being in this research study cost you?
All of the tests and procedures you will have during this study are considered standard of care treatment, including the blood tests and bone arrow aspirate and/or biopsies, for your disease and will be billed to you or your insurance company.

The study will pay for the Geriatric assessments, the Quality of Life assessments and the Neurocognitive assessments.

You will be responsible for any applicable insurance deductibles and co-payments. If you wish to speak with a financial counselor about your insurance coverage and benefits, let the investigator or other study personnel know. A contact for personal assistance will be made available for you.

Will you be paid for being in this research study?
You will not be paid to be in this research study.

Who is paying for this research?
This research is being paid for by the Department of Internal Medicine, Section of Oncology of the University of Nebraska Medical Center.

What should you do if you are injured or have a medical problem during this research study?
Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

The Institution has no plans to pay for any required treatment or provide other compensation. If you have insurance, your insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of your legal rights.

How will information about you be protected?
You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

Who will have access to information about you?
By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your PHI will be used only for the purpose(s) described in the section What is the reason for doing this research study?

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:
    - The HHS Office of Human Research Protections (OHRP)
    - The Food and Drug Administration (FDA)
    - National Institutes of Health (NIH)
- The HIPAA Privacy Rule requires the following groups to protect your PHI:
    - Your health insurance company
    - The Fed & Pamela Buffett Cancer Center Scientific Review Committee (SRC)

You are authorizing us to use and disclose your PHI for as long as the research study is being conducted.

You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?
In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address:
Vijaya Bhatt, M.D.
Principal Investigator
986840 Nebraska Medical Center
Omaha, NE 68198-6840

A description of this clinical trial will be available on 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 this website at any time.

What will happen if you decide not to be in this research study?
You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or the Institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?
You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff.

Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits to which you are entitled.

For your safety, please talk to the research team before you stop study related procedures.

You may be taken off the study if you do not follow instructions of the investigator or the research team.

You may also be taken off the study if

- Unacceptable toxicities
- Progressive Disease
- Investigator's discretion that it is in the best interest of the patient to withdraw
- Development of other medical problems that would make continuing on the study detrimental to your safety

Any research data obtained to date may still be used in the research.

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

What should you do if you have any questions about the study?
You have been given a copy of "*What Do I Need to Know Before Being in a Research Study?*" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your rights as a research participant?
You have rights as a research subject. These rights have been explained in this consent form and in "The Rights of Research Subjects" that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463.
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
    - Telephone: (402) 559-6941

- Email: unmcrsa@unmc.edu

Documentation of informed consent

You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of "The Rights of Research Subjects"
- You have had your questions answered.
- You have decided to be in the research study.

- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject _____
Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Signature of Person obtaining consent _____
Date _____

Authorized Study Personnel

Principal

* Bhatt, Vijaya
phone: 402-559-8008
alt #: 402-559-5174
degree: MD

Secondary

* Al-Kadhimi, Zaid
phone: 402-559-4013
alt #: 402-559-5520
degree: M.D.

* Armitage, James
phone: 402-559-7290
alt #: 402-888-7290
degree: M.D.

* Gundabolu, Krishna
phone: 402-559-8052
alt #: 402-559-8052
degree: MD

* Holstein, Sarah
phone: 402-559-6660
alt #: 402-559-8013
degree: MD

* Maness Harris, Lori
phone: 402-559-3742
alt #: 402-559-5520
degree: MD

* Vose, Julie
phone: 402-559-3848
alt #: 402-305-0790
degree: M.D.

Participating Personnel

Baljevic, Muhamed
alt #: 402-559-8013
degree: MD

* Bociek, Robert (Greg)
phone: 402-559-5388
alt #: 402-888-2630
degree: MD

* D'Angelo, Christopher
phone: 402-559-8110
alt #: 402-559-8013
degree: MD

* Kallam, Avyakta
phone: 402-559-0791
alt #: 402-913-4366
degree: MD

* Lunning, Matthew
phone: 402-559-7164
alt #: 402-559-7164
degree: DO

What Do I Need To Know Before Being In A Research Study?

You have been invited to be in a **research study**. Research studies are also called "clinical trials" or "protocols." **Research** is an organized plan designed to get new knowledge about a disease or the normal function of the body. The people who are in the research are called **research subjects**. The **investigator** is the person who is running the research study. You will get information from the investigator and the research team, and then you will be asked to give your **consent** to be in the research.

This sheet will help you think of questions to ask the investigator or his/her staff. You should know all these answers before you decide about being in the research.

What is the **purpose** of the research? Why is the investigator doing the research?

What are the **risks** of the research? What bad things could happen?

What are the possible **benefits** of the research? How might this help me?

How is this research different than the care or treatment I would get if I wasn t in the research? Are there other treatments I could get?

Does **everyone** in this research study get the same treatment?

Will being in the research **cost** me anything extra?

Do I have to be in this research study? Will the doctor still take care of me if I say **no**?

Can I **stop** being in the research once I ve started? How?

Who will look at my **records**?

How do I reach the investigator if I have more **questions**?

Who do I call if I have questions about being a **research subject**?

Make sure all your questions are answered before you decide whether or not to be in this research.

THE RIGHTS OF RESEARCH SUBJECTS
AS A RESEARCH SUBJECT YOU HAVE THE RIGHT

to be told everything you need to know about the research before you are asked to decide whether or not to take part in the research study. The research will be explained to you in a way that assures you understand enough to decide whether or not to take part.

to freely decide whether or not to take part in the research.

to decide not to be in the research, or to stop participating in the research at any time. This will not affect your medical care or your relationship with the investigator or the Nebraska Medical Center. Your doctor will still take care of you.

to ask questions about the research at any time. The investigator will answer your questions honestly and completely.

to know that your safety and welfare will always come first. The investigator will display the highest possible degree of skill and care throughout this research. Any risks or discomforts will be minimized as much as possible.

to privacy and confidentiality. The investigator will treat information about you carefully, and will respect your privacy.

... to keep all the legal rights you have now. You are not giving up any of your legal rights by taking part in this research study.

to be treated with dignity and respect at all times

The Institutional Review Board is responsible for assuring that your rights and welfare are protected. If you have any questions about your rights, contact the Institutional Review Board at (402) 559-6463.