A Study to Compare Standard Chemotherapy to Therapy With CPX-351 and/or Gilteritinib for Patients With Newly Diagnosed AML With or Without FLT3 Mutations

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 6 months to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- All patients must be enrolled on APEC14B1 and consented to Eligibility Screening (Part A) prior to enrollment and treatment on AAML1831. Bone marrow and/or blood must have been submitted to the BPC via APEC14B1 for testing of FLT3 markers. Patients without samples submitted for FLT3 testing are not eligible
- Patients must be at least 6 months of age and less than 22 years of age at the time of study enrollment
- Patient must be newly diagnosed with de novo AML according to the 2016 World Health Organization (WHO) classification with or without extramedullary disease
    - Patient must have 1 of the following:
    - >= 20% bone marrow blasts (obtained within 14 days prior to enrollment)
        - In cases where extensive fibrosis may result in a dry tap, blast count can be obtained from touch imprints or estimated from an adequate bone marrow core biopsy
    - < 20% bone marrow blasts with one or more of the genetic abnormalities associated with childhood/young adult AML as provided in the protocol (sample obtained within 14 days prior to enrollment)
    - A complete blood count (CBC) documenting the presence of at least 1,000/uL (i.e., a white blood cell [WBC] count >= 10,000/uL with >= 10% blasts or a WBC count of >= 5,000/uL with >= 20% blasts) circulating leukemic cells (blasts) if a bone marrow aspirate or biopsy is pending or cannot be performed (performed within 7 days prior to enrollment)
- ARM C: Patient must be >= 2 years of age at the time of Late Callback
- ARM C: Patient must have FLT3/ITD allelic ratio > 0.1 as reported by Molecular Oncology
- ARM C: Patient does not have any congenital long QT syndrome or congenital heart block
- ARM C: Females of reproductive potential must agree to use effective contraception during treatment and for at least 6 months after the last dose of gilteritinib
- ARM C: Lactating women must agree not to breastfeed during treatment with gilteritinib and for 2 months after the last dose of gilteritinib
- ARM C: Males of reproductive potential must agree to use effective contraception during treatment and for at least 4 months after the last dose of gilteritinib
- ARM D: Patient must be >= 2 years of age at the time of Late Callback
- ARM D: Patient must have one of the clinically relevant non-ITD FLT3 activating mutations as reported by Foundation Medicine
- ARM D: Females of reproductive potential must agree to use effective contraception during treatment and for at least 6 months after the last dose of gilteritinib
- ARM D: Lactating women must agree not to breastfeed during treatment with gilteritinib and for 2 months after the last dose of gilteritinib
- ARM D: Males of reproductive potential must agree to use effective contraception during treatment and for at least 4 months after the last dose of gilteritinib
- NEUROPSYCHOLOGICAL TESTING: Patient must be enrolled on Arm A or Arm B. Patients who transfer to Arm C or Arm D are not eligible
- NEUROPSYCHOLOGICAL TESTING: Patient must be 5 years or older at the time of enrollment
- NEUROPSYCHOLOGICAL TESTING: English-, French- or Spanish-speaking
- NEUROPSYCHOLOGICAL TESTING: No known history of neurodevelopmental disorder prior to diagnosis of AML (e.g., Down syndrome, fragile X, William syndrome, mental retardation)
- NEUROPSYCHOLOGICAL TESTING: No significant visual or motor impairment that would prevent computer use or recognition of visual test stimuli
- All patients and/or their parents or legal guardians must sign a written informed consent
- All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met

Exclusion Criteria:

- Fanconi anemia

- Shwachman Diamond syndrome
- Patients with constitutional trisomy 21 or with constitutional mosaicism of trisomy 21
- Telomere disorders
- Germline predispositions known, or suspected by the treating physician to increase risk of toxicity with AML therapy
- Any concurrent malignancy
- Juvenile myelomonocytic leukemia (JMML)
- Philadelphia chromosome positive AML
- Mixed phenotype acute leukemia
- Acute promyelocytic leukemia
- Acute myeloid leukemia arising from myelodysplasia
- Therapy-related myeloid neoplasms
- Patients with persistent cardiac dysfunction prior to enrollment, defined as ejection fraction (EF) < 50% (preferred method Biplane Simpson's EF) or if EF unavailable, shortening fraction (SF) < 24%. *Note: if clinically safe and feasible, repeat echocardiogram is strongly advised in order to confirm cardiac dysfunction following clinical stabilization, particularly if occurring in the setting of sepsis or other transient physiologic stressor. If the repeat echocardiogram demonstrates an EF >= 50%, the patient is eligible to enroll and may receive an anthracycline-containing Induction regimen
- Administration of prior anti-cancer therapy except as outlined below:
    - Hydroxyurea
    - All-trans retinoic acid (ATRA)
    - Corticosteroids (any route)
    - Intrathecal therapy given at diagnosis
    - In particular, strong inducers of CYP3A4 and/or P-glycoprotein (P-gp) should be avoided from the time of enrollment until it is determined whether the patient will receive gilteritinib. Patients receiving gilteritinib will be required to avoid strong CYP3A4 inducers and/or strong P-gp inducers for the duration of the study treatment
- Patients < 8.3 kg at study enrollment are not eligible
- Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential
- Lactating females who plan to breastfeed their infants
- Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation
- ARM D: Patient does not have any congenital long QT syndrome or congenital heart block

Conditions & Interventions

Interventions:
PROCEDURE: Allogeneic Hematopoietic Stem Cell Transplantation, DRUG: Asparaginase Erwinia chrysanthemi, PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Computed Tomography, DRUG: Cytarabine, DRUG: Daunorubicin Hydrochloride, DRUG: Dexrazoxane Hydrochloride, DRUG: Etoposide, OTHER: Fludeoxyglucose F-18, DRUG: Gemtuzumab Ozogamicin, DRUG: Gilteritinib Fumarate, DRUG: Liposome-encapsulated Daunorubicin-Cytarabine, PROCEDURE: Magnetic Resonance Imaging, DRUG: Methotrexate, DRUG: Mitoxantrone Hydrochloride, PROCEDURE: Positron Emission Tomography, OTHER: Questionnaire Administration, DRUG: Therapeutic Hydrocortisone
Conditions:
Acute Myeloid Leukemia

More Information

Description:
This phase III trial compares standard chemotherapy to therapy with liposome-encapsulated daunorubicin-cytarabine (CPX-351) and/or gilteritinib for patients with newly diagnosed acute myeloid leukemia with or without FLT3 mutations. Drugs used in chemotherapy, such as daunorubicin, cytarabine, and gemtuzumab ozogamicin, work in different ways to stop the growth of cancer cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. CPX-351 is made up of daunorubicin and cytarabine and is made in a way that makes the drugs stay in the bone marrow longer and could be less likely to cause heart problems than traditional anthracycline drugs, a common class of chemotherapy drug. Some acute myeloid leukemia patients have an abnormality in the structure of a gene called FLT3. Genes are pieces of DNA (molecules that carry instructions for development, functioning, growth and reproduction) inside each cell that tell the cell what to do and when to grow and divide. FLT3 plays an important role in the normal making of blood cells. This gene can have permanent changes that cause it to function abnormally by making cancer cells grow. Gilteritinib may block the abnormal function of the FLT3 gene that makes cancer cells grow. The overall goals of this study are, 1) to compare the effects, good and/or bad, of CPX-351 with daunorubicin and cytarabine on people with newly diagnosed AML to find out which is better, 2) to study the effects, good and/or bad, of adding gilteritinib to AML therapy for patients with high amounts of FLT3/ITD or other FLT3 mutations and 3) to study changes in heart function during and after treatment for AML. Giving CPX-351 and/or gilteritinib with standard chemotherapy may work better in treating patients with acute myeloid leukemia compared to standard chemotherapy alone.

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