MT2020-35 - COG AAML1831 - A Phase 3 Randomized Trial for Patients With De Novo AML Comparing Standard Therapy Including Gemtuzumab Ozogamicin (GO) to CPX-351 With GO, and the Addition of the FLT3 Inhibitor Gilteritinib for Patients With FLT3 Mutations

Status: Recruiting

Eligibility Criteria

Sex: All
Age: up to 22 Years old
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. Submission of diagnostic specimens must be done according to the Manual of Procedures

• Patients must be 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 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

• 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, Drug: Asparaginase Erwinia chrysanthemi, Behavioral: Cogstate Assessment Battery, Drug: Cytarabine, Drug: Daunorubicin Hydrochloride, Drug: Dexrazoxane Hydrochloride, Drug: Etoposide, Drug: Gemtuzumab Ozogamicin, Drug: Gilteritinib Fumarate, Drug: Liposome-encapsulated Daunorubicin-Cytarabine, Drug: Methotrexate, Drug: Mitoxantrone Hydrochloride, Drug: Therapeutic Hydrocortisone

Conditions:

Acute Myeloid Leukemia

More Information

Description: The overall goal of this study is 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, and to find out what effects, good and/or bad, the drug gilteritinib has when given with chemotherapy to children and young adults with newly diagnosed AML and the FLT3/ITD mutation or non-ITD FLT3 activating mutations.

Contact(s): Allison Fullenkamp - fulle631@umn.edu

Principal Investigator: Peter Gordon

Phase: Phase 3

IRB Number: STUDY00010751

System ID: NCT04293562
