

# 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

**Age:** Up to 21 years old

This study is NOT accepting healthy

**Healthy Volunteers:** volunteers

### Inclusion Criteria:

\* All patients must be enrolled on APEC14B1 and consented to Eligibility Screening (Part A) prior to enrollment and treatment on AAML1831 \* 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: \*  $\geq 20\%$  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  $\geq 10,000/uL$  with  $\geq 10\%$  blasts or a WBC count of  $\geq 5,000/uL$  with  $\geq 20\%$  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  $\geq 2$  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  $\geq 2$  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  $\geq 50\%$ , 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 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

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**Phase:** PHASE3

**IRB**

**Number:** HM20020887

**System ID:** NCT04293562

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