

**CALGB 10603: A Phase III Randomized, Double-Blind Study of Induction (Daunorubicin/
Cytarabine) and Consolidation (High-Dose Cytarabine) Chemotherapy + Midostaurin (PKC412)
(IND # 101261) or Placebo in Newly Diagnosed Patients < 60 Years of Age with FLT3 Mutated Acute
Myeloid Leukemia (AML)**

Fast Facts

ELIGIBILITY CRITERIA

- 1) Unequivocal diagnosis of AML (>20% blasts in the bone marrow based on the WHO classification), excluding M3 (acute promyelocytic leukemia). Patients with neurologic symptoms suggestive of CNS leukemia are recommended to have a lumbar puncture. Patients whose CSF is positive for AML blasts are not eligible
- 2) Documented FLT3 mutation (ITD or point mutation), determined by analysis in protocol – designated FLT3 screening laboratory (see section 6.0)
- 3) Age \geq 18 and < 60 years.
- 4) Prior therapy:
 - a) No prior chemotherapy for leukemia or myelodysplasia with the following exceptions:
 - i. Emergency leukapheresis
 - ii. Emergency treatment for hyperleukocytosis with hydrxyurea for \leq 5 days
 - iii. Cranial RT for CNS leukostasis (one dose only)
 - iv. Growth factor / cytokine support
 - b. AML patients with a history of antecedent myelodysplasia (MDS) remain eligible for treatment on this trial, but must not have had prior cytotoxic therapy (eg azacitidine or decitabine)
 - c. Patients who have developed therapy related AML after prior RT or chemotherapy for another cancer or disorder are not eligible.
- 5) Patients with symptomatic congestive heart failure are not eligible.
- 6) Bilirubin < 2.5 ULN
- 7) Women with child bearing potential and must have serum or urine pregnancy test to a sensitivity of 50 mIU/mL with in 16 days of registration.
- 8) Women may not be pregnant or nursing. Sexually active women must use two adequate forms of birth control during treatment and for 12 weeks after therapy has ended (oral contraceptives are not considered adequate birth control due to possible midostaurin interaction) Sexually active men must use a condom during treatment and for 12 weeks after therapy as ended. (see section 4.6 for further details).
- 9) All patients must be informed of the investigational nature of this study and give written informed consent according to institutional and federal guidelines

The following are to be taken into consideration when enrolling patients, but are not eligibility criteria:

- 10) No other serious illnesses which would limit survival to < 2 years.
- 11) No psychiatric condition which would prevent compliance with treatment or informed consent.
- 12) No uncontrolled or severe angina, diabetes, infection or pulmonary disease, which in the opinion of the investigator would make this protocol treatment unreasonably hazardous for the patient.
- 13) Patients may not have a “currently active” second malignancy other than non-melanoma skin cancer.
- 14) Physicians should be aware that midostaurin is a competitive inhibitor of CYP3A4/5. Studies also show CYP3A4/5 is the major human p450 enzyme catalyzing biotransformation of midostaurin. A list of agents that may have potential drug interactions is included in Appendix I.

PRE-STUDY PARAMETERS

- 1) History and physical with height, weight and performance status.
- 2) CBC with differential, CMP including uric acid and magnesium, PT (INR), PTT, fibrinogen, urinalysis, thyroid function tests (T4 & TSH), U-HCG or serum HCG.
- 3) LVEF (Echo or MUGA)
- 4) Chest x-ray, PA & lateral
- 5) Bone marrow aspirate (cytogenetics)

TREATMENT

