

## PROTOCOL CARD, CALGB 10603

**Leukemia**  
Version Date 12/1/09

### 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)

#### Eligibility

- Patients with unequivocal diagnosis of AML (> 20% blasts in the bone marrow based on the WHO classification), excluding M3 (acute promyelocytic leukemia).
- Patients with symptoms suggestive of CNS leukemia are recommended to have an LP; patients whose CSF is positive for AML blasts are not eligible.
- Patients must have documented FLT3 mutation (ITD or point mutation), determined by analysis in a protocol-designated FLT3 screening laboratory.
- Patients must be  $\geq 18$  and < 60 years of age.
- Patients must not have had prior chemotherapy for leukemia or myelodysplasia except for: emergency leukapheresis, emergency treatment for hyperleukocytosis with hydroxyurea for  $\leq 5$  days, cranial RT for CNS leukostasis (one dose only), or growth factor/cytokine support.
- Patients who have a history of antecedent MDS remain eligible for this trial, but must not have had prior cytotoxic therapy (e.g., azacitidine or decitabine).
- Patients must not have developed therapy-related AML after prior RT or chemotherapy for another cancer or disorder.
- Patients must not have symptomatic CHF.
- Patients must not be pregnant or nursing. Women of childbearing potential must commit to abstinence or use two acceptable methods of birth control during and after the study, and men must agree not to father a child and must use a latex condom during and after the study.

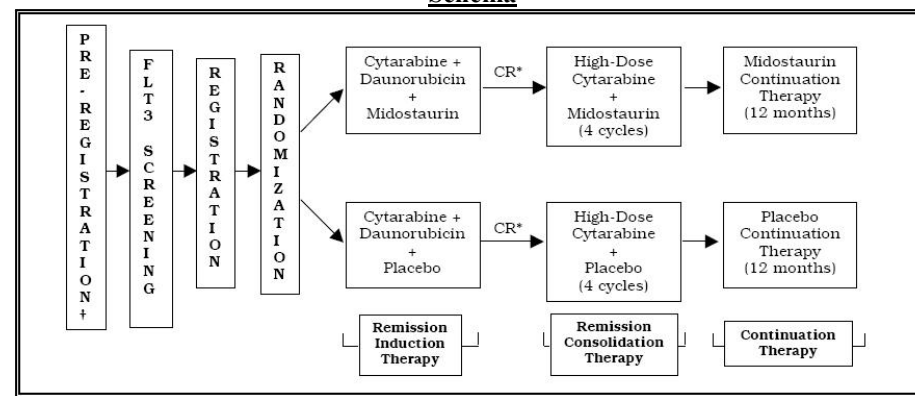
The following are not formal eligibility criteria, but should be taken into account when considering patients for the trial:

- Other serious illnesses that would limit survival to < 2 years
- Psychiatric conditions which would prevent compliance
- Uncontrolled or severe angina, diabetes, infection, or pulmonary disease which, in the opinion of the treating physician, would make the protocol treatment unreasonably hazardous for the patient
- "Currently active" second malignancy other than non-melanoma skin cancers
- Concomitant use of medications that are potent inducers or inhibitors of the CYP3A4/5.

**THIS INFORMATION IS INTENDED TO BE USED AS A SCREENING TOOL ONLY AND SHOULD NOT BE USED IN PLACE OF THE PROTOCOL.**

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#### Schema



(See protocol for footnotes)

#### Required Bloodwork and Tests

(H&P, blood work and CXR within 16 days prior to registration; Baseline exams for screening, i.e., LVEF or MUGA, within 42 days prior to registration)

- History and Physical
- CBC/diff, Platelets
- BUN, Creatinine, Electrolytes
- ALT/AST, Alk. Phos.
- Bilirubin < 2.5 x ULN
- Uric Acid, Ca<sup>++</sup>, Glucose, Mg
- Total Protein, Albumin
- PT(INR), PTT, Fibrinogen
- UA
- Thyroid Function Tests (T4 & TSH)
- LVEF (MUGA or ECHO)
- U-HCG or serum HCG women of childbearing potential
- Chest x-ray, PA and Lateral
- Bone Marrow Aspirate
- Cytogenetics prior to initiation of therapy
- Central Morphology Review
- Lumbar Puncture if indicated by neurological symptoms