CALBG10404: A Genetic, Risk Stratified Randomized Phase II study of Four Fludarabine/Antibody Combinations for Patients with Symptomatic, Previously Untreated Chronic Lymphocytic Leukemia.

MAJOR ELIGIBILITY CRITERIA:

- Must have a specific diagnosis of B-Cell CLL
- Absolute lymphocytosis of > 5,000 / µL
- Must have symptomatic and active **intermediate or high-risk categories of the modified three-stage Rai staging system**
- Must have evidence of active disease if in the intermediate-risk group as demonstrated by ≥ 1 of following:
  - Massive or progress splenomegaly, hepatomegaly and/or lymphadenopathy
  - Weight loss > 10% in last 6 months
  - Grade 2 or 3 fatigue
  - Fevers > 100.5° or night sweats for > 2 weeks w/o evidence of infection
  - Progressive lymphocytosis w/ an increase of >50% over a 2 month period or an anticipated doubling time of less than 6 months
- No prior therapy for CLL (no corticosteroids for autoimmune complications following intial diagnosis of CLL)
- No medical condition requiring chronic use of oral corticosteroids
- At least 18 years old
- Performance Status 0-2
- No HIV unless:
  - No evidence of infection with hepatitis B or C
  - CD4+ cell count > 350/mm^3
  - No evidence of resistant strains of HIV
  - If not on anti-HIV therapy, an HIV viral load < 10,000 copies HIV RNA/mL
  - If on HIV therapy, HIV viral load < 50 copies HIV RNA/mL
  - No history of AIDS-defining condition
- Patients with HIV cannot be receiving concurrent zidovudine or stavudine
- Must be non-pregnant and non-nursing
- Creatinine ≤ 1.5 x upper limit of normal

PRE-STUDY LABS AND TESTS:

≤ 16 days prior to registration: all blood work, history & physical

-CBC, Diff, Platelets, Serum Creatinine, creatinine clearance, BUN, serum electrolytes, uric acid, glucose, phosphate, Calcium, AST, ALT, Alk. Phos., Bili, LDH, Albumin, Thyroid Function Tests (T3, T4, TSH), Quantitative Immunoglobulins, DAT, β2 Microglobulin, Serum or Urine HCG, PB immunophenotyping (CD5, CD19, CD23, CD52, surface immunoglobulins), CD4, CD8 & CD19

-Varicella Zoster IgG & CMV IgG (optional but strongly recommended)

-HBsAg, HBsAb, Hep C, HB core antibody (patients at high risk for Hep. B should be screened)

≤ 42 days prior to registration: CT Scan (chest, abdomen, & pelvis), Correlative Science Sample Submission, Bone Marrow Aspirate & Biopsy, Central Histologic Review

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