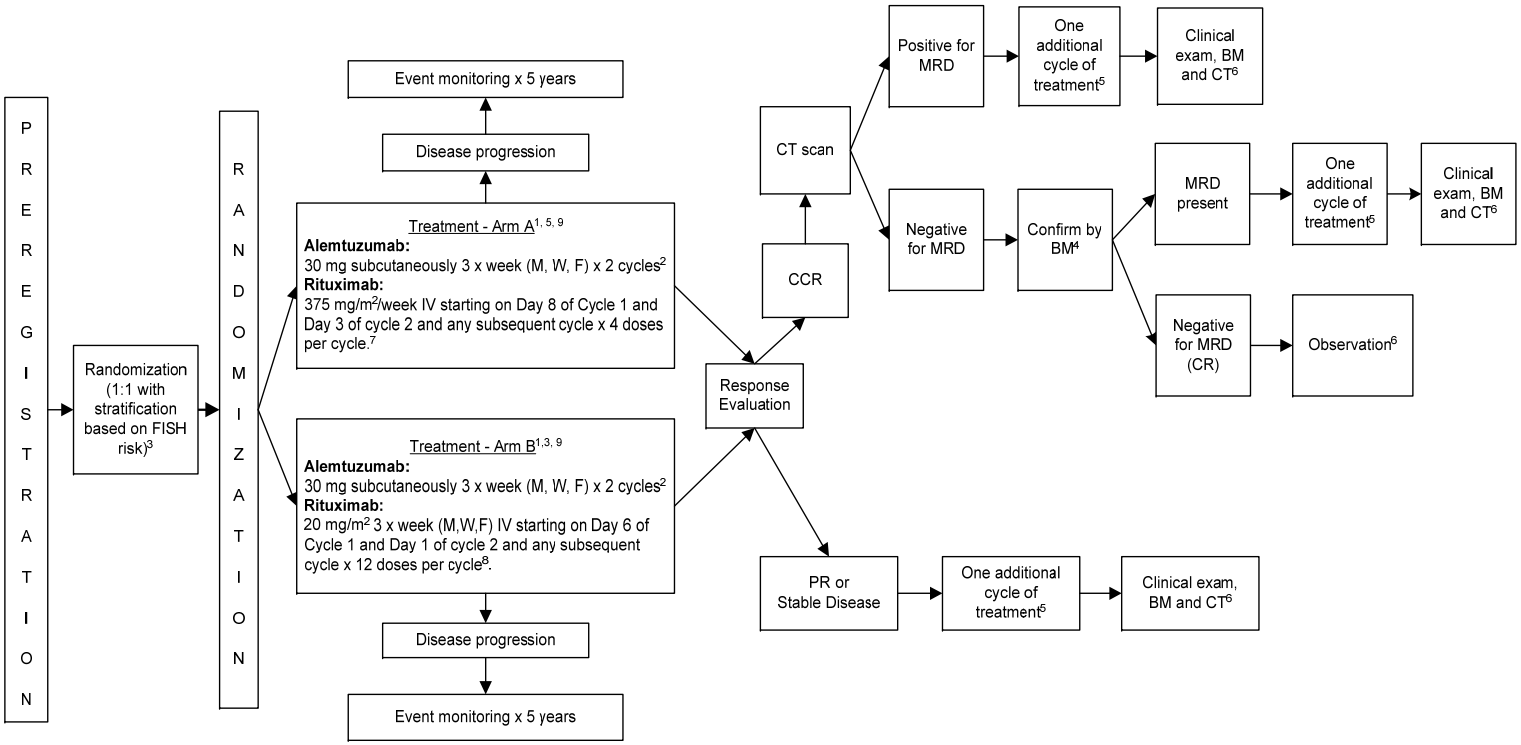
Schema



Accrual Goal: 90 Patients
Day 1 is Wednesday, for each cycle.

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1 Cycle 1 = 32 Days. Cycle 2 = 28 days. Additional cycles = 28 days.

2 Alemtuzumab dose for Cycle 1 Week 1 of both Arms A and B requires a 'dose ramp'. See Sections 5.1.1 and 5.2.1.

3 FISH risk status must be determined by the ECOG Cytogenetic Laboratory at Mayo Clinic. Submission of pre-study peripheral blood or bone marrow is mandatory to determine treatment stratification. See Section 10.1.

4 Bone marrow must be submitted after completion of two cycles of therapy in patients who have achieved clinical complete response. Central review will be done at Mayo Clinic and results will determine if patient will receive another cycle of therapy. See Section 10.2.1.

5 One additional cycle of treatment may be offered if the response evaluation shows CR with MRD, or PR, or stable. This third cycle will follow the treatment pattern of Cycle 2, i.e., 28 days, no dose ramp.

6. Patients will continue in observation for one year after completion of therapy in non-relapsing patients and then will be monitored for 5 years after study entry.

7. See Section 5.1.2 for dose days.

8. See Section 5.2.2 for dose days.

9. Alemtuzumab and rituximab can be given on sequential days - e.g. Tu-W-F or M-W-Th. Sequential day dosing can be given if patients cannot be treated on a specific day for logistical reasons.

E1908: A Phase II Randomized Trial Comparing Standard and Low Dose Rituximab: Initial Treatment of Progressive Chronic Lymphocytic Leukemia in Elderly Patients Using Alemtuzumab and Rituximab.

MAJOR ELIGIBILITY CRITERIA:

- Age > 70 years
- Must have dx of CLL with:
  - Minimum Peripheral Lymphocyte count of 5 x 10^9 /L OR palpable adenophathy > 1cm or palpable splenomegaly **AND**:
    - Immunophenotypic demonstrations of a population of B-Lymphocytes which are monoclonal . CLL will be Diagnosed if these cells have > 3 of the following Characteristics:
      - CD5+
      - CD23+
      - Dim surface light chain expression
      - Dim surface CD20 expression
    - FISH analysis is negative for IGH/CCND1 and/or immunostaining is degative for cyclin D1 expression to exclude Mantle Cell Lymphoma
- Must not have had any prior Treatment.
- Must have progressive CLL defined by at least one of the following:
  - Weight loss > 10% within the previous 6 months
  - Extreme fatigue (Gr3)
  - Fevers > 100.3 for 2 weeks w/o evidence of infection
  - Night Sweats
  - Evidence of progressive bone marrow failure with hemoglobin < 11 g/dL or Platelet count< 100, 000/uL
  - Rapidly progressive lymphadenopathy providing that the largest node is not > 5 cm in any dimension
- Adequate organ function
  - Creatinine < 2 x ULN
  - Total Bilirubin < 1.5 x ULN
  - AST < 3.0 x ULN (unless due to CLL involvement of the Liver
- Performance Status 1-3
- No massive Splenomegly > 6 cm below left costal margin
- No lymphadenopathy > 5cm in any diameter
- Must NOT have any of the following:
  - NY Heart Association Class III or IV heart disease
  - Recent myocardial infarction (<1 month prior to registration)
  - Uncontrolled infection
  - Infection with the HIV
  - Active Hep B
  - Positive Hep C serology
- Must NOT have evidence of active Autoimmune hemolytic anemia, Immune Thrombocytopenia, or pure red blood cell aplasia
- No other primary malignancy.
- No Concomitant use of continuous systemic corticosteroids

PRE-STUDY LABS AND TESTS:

≤14 days prior to study drug: CBC w/ diff, Creatinine, Total bili, LDH, Uric Acid, Sodium, Potassium, Phosphate, ALT, AST, COOMBS test, CMV DNA by PCR, HBsAg, CT and Bone Marrow Bx w/ Cytogenics

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