Cancer Research Consortium of West Michigan
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FAST FACTS

A041501 - A PHASE III TRIAL TO EVALUATE THE EFFICACY OF THE ADDITION OF INOTUZUMAB OZOGAMICIN (A CONJUGATED ANTI-CD22 MONOCLONAL ANTIBODY) TO FRONTLINE THERAPY IN YOUNG ADULTS (AGES 18-39 YEARS) WITH NEWLY DIAGNOSED PRECURSOR B-CELL ALL

Pre-registration Eligibility Criteria (Step 0)

1. **Bone marrow submission for LDA Assay**
   Submission of bone marrow aspirate for LDA assay is mandatory prior to registration for stratification. It should be initiated as soon as possible after pre-registration. The specimen should be sent as outlined in Section 6.2.2.
   Please note: Bone marrow aspirate and peripheral blood should also be submitted at this time for central MRD analysis and FISH as outlined in Section 6.2.3.

Registration Eligibility Criteria (Step 1)

1. **Documentation of Disease:**
   - Newly diagnosed patients with CD-22 positive B-cell acute lymphoblastic leukemia (WHO criteria) are eligible. Patients with Burkitt type ALL are NOT eligible.
   - Patients who have BCR-ABL fusion transcript determined by FISH or RT-PCR or t(9;22)(q34;q11) by cytogenetics are not eligible and should be considered for enrollment on studies that incorporate imatinib during induction.

   Please note: Patients must also be assessed for CD20 positivity and other markers as outlined in Section 5.0.

   Positivity for CD22 and CD20 is defined as baseline expression of the CD22 or CD20 antigen in more than 20% of leukemic cells using local multiparameter flow-cytometric immunophenotyping with the use of CD45 expression as a marker to gate the ALL blast population, according to recommendations from the European LeukemiaNet.

2. **Prior Treatment**
   - No prior therapy for ALL except for limited treatment (≤ 7 days) with corticosteroids or hydroxyurea and a single dose of intrathecal cytarabine. However, patients who are being treated with chronic steroids for other reasons (for example, to treat asthma, autoimmune disorders, lupus, etc.) are eligible.
   - No prior therapy for acute leukemia except emergency therapy (corticosteroids or hydroxyurea) for blast cell crisis, superior vena cava syndrome, or renal failure due to leukemic infiltration of the kidneys. When indicated, leukapheresis or exchange transfusion is recommended to reduce the WBC.
   - Single-dose intrathecal cytarabine is allowed prior to registration or prior to initiation of systematic therapy for patient convenience. This is usually done at the time of the

diagnostic bone marrow or venous line placement to avoid a second lumbar puncture. Systemic chemotherapy must begin within 72 hours of this intrathecal therapy.

3. **Not pregnant and not nursing,** because this study involves agents that have known genotoxic, mutagenic and teratogenic effects.
   Therefore, for women of childbearing potential only, a negative urine or serum pregnancy test done ≤ 8 days prior to registration is required.
4. **Age ≥ 18 years and < 40 years**
5. **ECOG Performance Status 0-2**
6. **Patients with Down Syndrome are excluded from this study** due to the likelihood of excessive toxicity resulting. These patients should be treated in consultation with a pediatric oncologist.
7. **Lab Values**

AST, ALT	≤ 3 x upper limit of normal (ULN), unless suspected leukemic involvement of the liver
Direct Bilirubin	≤ 3 x upper limit of normal (ULN), unless suspected leukemic involvement of the liver
Calc. Creatinine Clearance	≥ 50 mL/min by Cockcroft-Gault

Randomization Eligibility Criteria (Step 2)

1. **Completion of remission induction therapy (per Section 7.2).**
2. **Patients with M2 marrow or better (see table below) are eligible.** Patients with M3 or M4 marrow (greater than 25% lymphoblasts) will not be eligible to be randomized.

Rating	Blast Cells (%)*
M_0	0 – 5.0
M_1	0 – 5.0
M_2	5.1 – 25.0
M_3	>25.0 – 50.0
M_4	> 50.0

* The term "blast cell" includes any cell that cannot be classified as a more mature normal element, and includes "leukemic cells," pathologic lymphocytes, and stem cells.

3. **Lab Values**

Absolute Neutrophil Count (ANC)	≥ 750/mm^3
Platelet Count	≥ 75,000/mm^3
Total Bilirubin	≤ 1.5 x upper limit of normal (ULN), except for patients with known Gilbert's syndrome
AST	≤ 8 x upper limit of normal (ULN)

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PATIENT ENROLLMENT PATHWAY

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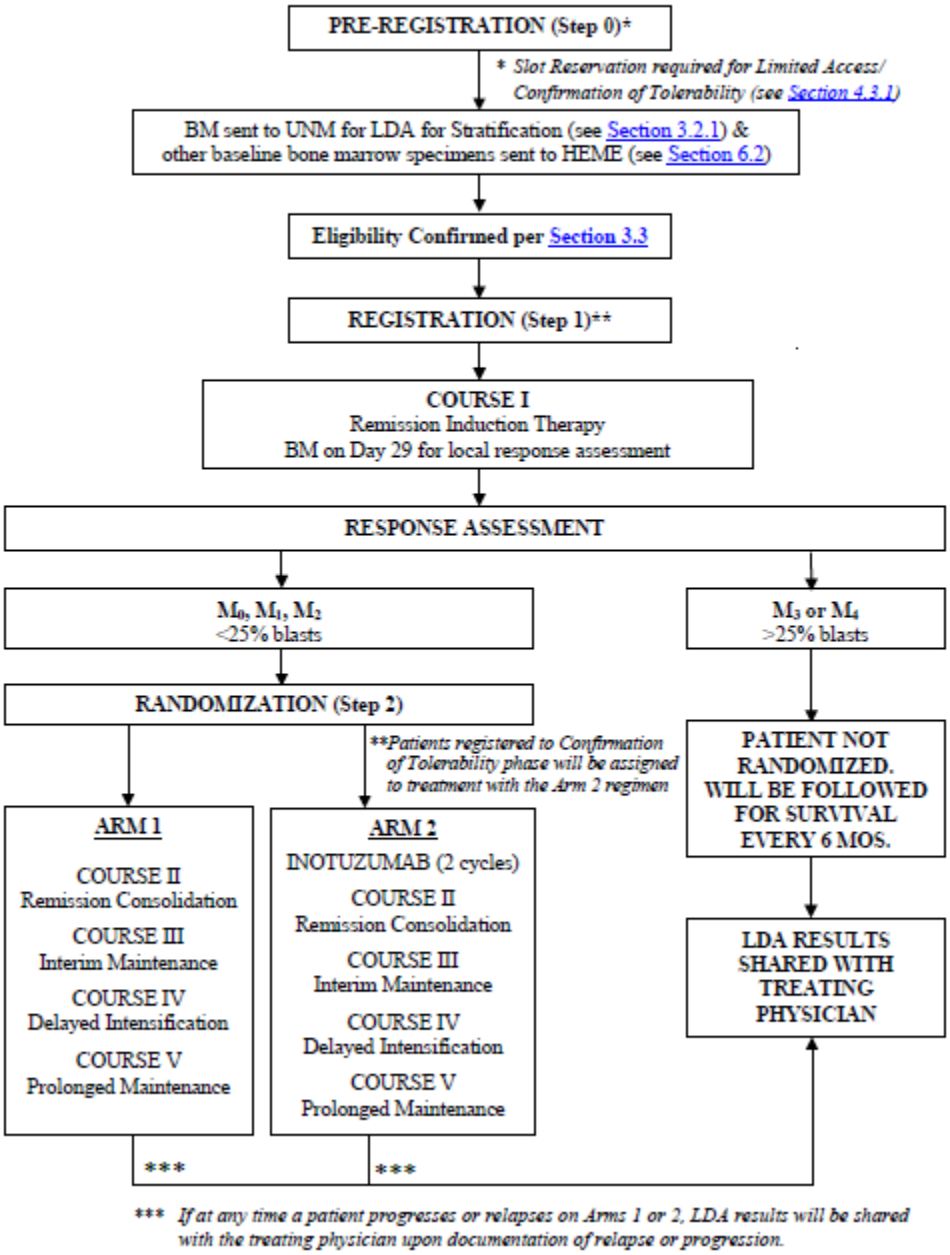

*** *If at any time a patient progresses or relapses on Arms 1 or 2, LDA results will be shared with the treating physician upon documentation of relapse or progression.*