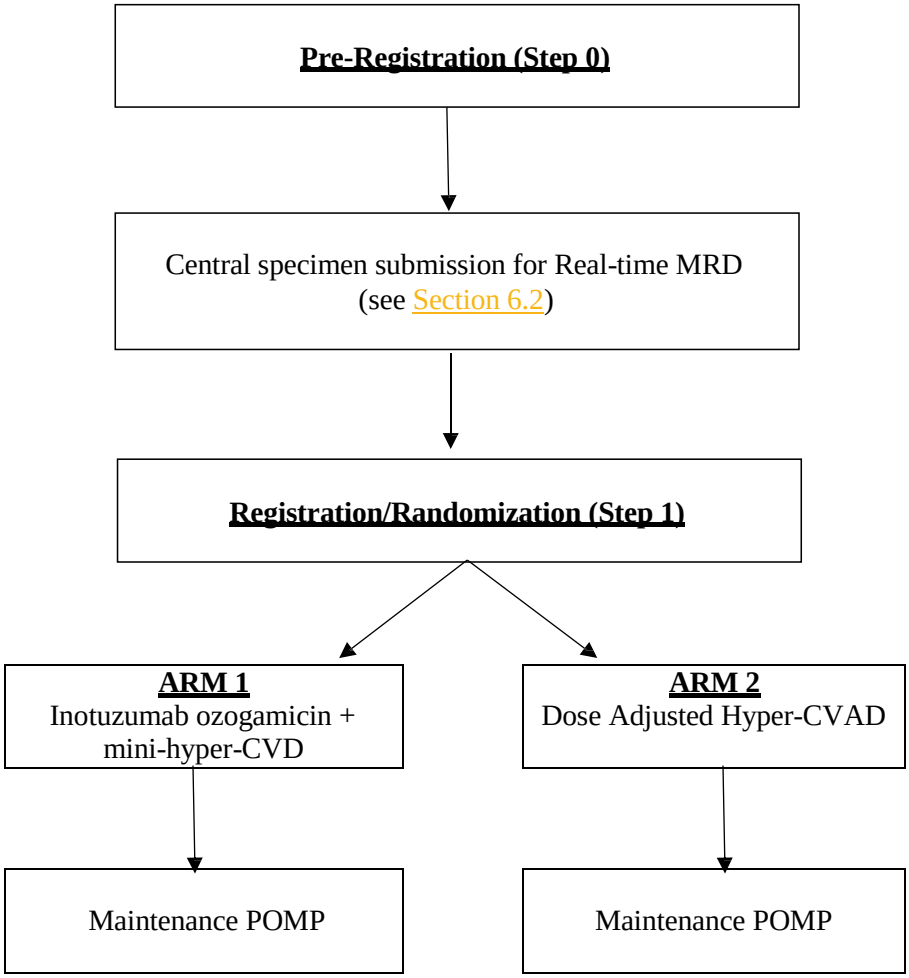
Schema

1 Cycle = 28 Days



Treatment is to continue until disease progression, unacceptable adverse event, or allogeneic stem cell transplantation. Patients will be followed for 5 years or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

3.0 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.1 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Physicians should consider whether any of the following may render the patient inappropriate for this protocol:

- Medical condition such as uncontrolled diabetes mellitus, uncontrolled cardiac disease, and uncontrolled pulmonary disease.
- Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.
- Patients with a "currently active" second malignancy other than non-melanoma skin cancers, early stage prostate cancer, cervical carcinoma *in situ*, or other cancer for which standard of care would be observation (not requiring treatment). Patients are not considered to have a "currently active" malignancy if they have completed therapy and are free of disease for ≥1 year, or if the cancer has been surgically resected and considered cured. Patients with a history of multiple myeloma with absence of serum paraprotein for ≥1 year are not considered to have a "currently active" malignancy.

In addition:

- Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study due to the teratogenic potential of the therapy utilized in this trial. Include as applicable: Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives, or double barrier method (diaphragm plus condom).

3.2 Pre-Registration Eligibility Criteria (Step 0)

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

3.2.1 Research bone marrow or peripheral blood submission

This bone marrow or peripheral blood submission is mandatory prior to registration/randomization as baseline for real-time MRD analysis. The bone marrow sample should be from the first aspiration (i.e., first pull). Aspirate needle should be redirected if needed to get first pull bone marrow aspirate. It should be obtained as soon after pre-registration as possible.

3.3 Registration Eligibility Criteria (Step 1)

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is

considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

___ **3.3.1 Disease Histologic Documentation:**

Diagnosis of B-cell ALL or LBL per WHO 2016 criteria. Patients must have ≥5% blasts in the bone marrow or blood. Patients with lymphoblastic lymphoma (LBL) without measurable marrow involvement (≥5% blasts) are not eligible.

- T-cell ALL/LBL, Philadelphia-chromosome positive B-cell (as determined by FISH, cytogenetics, or RT-PCR), and Burkitt's like leukemia/lymphoma (mature B-ALL) are not eligible.

___ **3.3.2 CD22 positive:** Must be CD22 positive by *local* assessment (≥20% by immunohistochemistry or flow cytometry). Patients are eligible regardless of CD20 status but CD20 expression should be assessed at diagnosis by flow cytometry or immunohistochemistry.

___ **3.3.3 Patients with symptomatic CNS disease are not eligible.** CNS assessment is not required for eligibility determination if asymptomatic.

___ **3.3.4 Measurable disease:** Patients must have ≥5% blasts in the bone marrow or blood. Patients with lymphoblastic lymphoma (LBL) without marrow involvement (≥5% blasts) are not eligible.

___ **3.3.5 Prior Treatment**

No prior chemotherapy for ALL except for hydroxyurea (no limit), steroids limited to 7 days, ATRA (no limit), vincristine (single dose), and/or intra-thecal chemotherapy. Leukapheresis is permitted. Palliative radiation to doses 24 Gy or less is permitted. Patients being treated with chronic steroids for other reasons (autoimmune disorder, etc.) are eligible.

___ **3.3.6 Age ≥ 50 years**

___ **3.3.7 ECOG Performance Status ≤ 2. ECOG 3 permitted if related to disease.**

___ **3.3.8 Required Initial Laboratory Values and Studies:**

Creatinine	≤ 2.0 g/dL
Total Bilirubin	≤ 1.5 x upper limit of normal (ULN)*
	* Except in the event of: 1) Gilbert disease, in which case total bilirubin must be ≤ 2 x ULN, or 2) elevated bilirubin believed by investigator to be due to leukemic infiltration, in which case total bilirubin must be ≤ 2 x ULN.
AST / ALT	≤ 2.5 x upper limit of normal (ULN)
Cardiac Ejection Fraction (As measured by MUGA or echocardiogram)	> 40%

___ **3.3.9 No clinically relevant liver disease** (such as cirrhosis, active hepatitis, or alcohol use disorder), which in the opinion of the treating physician would make this protocol unreasonably hazardous.

- Patients with known hepatitis B virus (HBV) infection are eligible if they are on effective HBV suppressive therapy with undetectable HBV viral load and there is no clinically relevant liver disease present (related or unrelated to HBV-related liver damage).
- Patients with known history of hepatitis C virus (HCV) infection are eligible if they have cleared the infection spontaneously or via eradication therapy (HCV viral load undetectable) and there is no clinically relevant liver disease present (related or unrelated to HCV-related liver damage).