

**COG-AALL02P2: Treatment of Late Isolated Extramedullary Relapse from Acute Lymphoblastic Leukemia (ALL)
(Initial CR1 \geq 18 months)**

PATIENT ELIGIBILITY:

Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient's medical/research record which will serve as the source document for verification at the time of audit.

- ___ 1. Study enrollment must take place within five calendar days of beginning protocol therapy. If enrollment takes place before starting therapy, the date protocol therapy is projected to start must be no later than five (5) calendar days after enrollment.
- ___ 2. Patient must be \geq 18 months and $<$ 30 years of age at time of relapse.
- ___ 3. Diagnosis of ALL (either B-precursor or T-Lineage) in first BM remission with first isolated CNS and/or testicular relapse, or diagnosis of Lymphoblastic NHL with first isolated CNS and/or testicular relapse. Length of initial complete remission must be \geq 18 months from the time of initial diagnosis. Bone marrow must be M1 by morphology.
- ___ 4. CNS Relapse is defined as
At least 5WBCS/ μ l in CSF with blasts present on cytopsin.
Any number of WBC in CSF with immunophenotypic proof of leukemic relapse. Immunophenotypic proof of relapse is defined as identifiable blasts **plus** B-lineage: TdT or CD-10 positivity on 2 consecutive CSF samples four weeks apart **OR** T-lineage: TdT and CD-7 or TdT positivity alone on 2 consecutive CSF samples four weeks apart.
- ___ 5. Testicular Relapse is defined as
Biopsy proven testicular involvement.
- ___ 6. Patient must have a performance score of \geq 30. Use Karnofsky for patients $>$ 16 years of age and Lansky for patients \leq 16 years of age.
- ___ 7. Prior Therapy
 - Patient should not have had prior (non-protocol specified) systemic therapy for current extramedullary relapse. IT therapy given within one week of beginning systemic Induction will be considered Day 1 dose of ITT.
 - Total anthracycline dosage must be \leq 360 mg/m².
- ___ 8. Concomitant Medications Restrictions - None.

___9. Organ Function Requirements

- Patient must have adequate renal function defined as:
 - Creatinine clearance or radioisotope GFR $\geq 70\text{ml/min/1.73m}^2$, OR
 - A serum creatinine based on age/gender as follows:

Age	Maximum Serum Creatinine (mg/dL)	
	Male	Female
1 month to < 6 months	0.4	0.4
6 months to < 1 year	0.5	0.5
1 to < 2 years	0.6	0.6
2 to < 6 years	0.8	0.8
6 to < 10 years	1	1
10 to < 13 years	1.2	1.2
13 to < 16 years	1.5	1.4
≥ 16 years	1.7	1.4

The threshold creatinine values in this Table were derived from the Schwartz formula for estimating GFR (Schwartz et al. J. Peds, 106:522, 1985) utilizing child length and stature data published by the CDC.

- Patient must have adequate cardiac function defined as:
 - Shortening fraction of $\geq 27\%$ by echocardiogram, or
 - Ejection fraction of $\geq 50\%$ by radionuclide angiogram (MUGA).

EXCLUSION CRITERIA:

- ___1. Patients with Down syndrome are not eligible due to increased sensitivity to MTX.
- ___2. Patients who have had a BMT in first remission are not eligible.
- ___3. Patients with known optic nerve and or retinal involvement are not eligible (because they are unable to delay XRT for 12 months). Patients presenting with visual disturbances should have an ophthalmological exam and, if indicated, an MRI to determine optic nerve or retinal involvement.

REQUIRED OBSERVATIONS:

Required Clinical Laboratory and Disease Evaluations for all patients (CNS and Testicular relapse)

- Hx/PE (Wt, Neurol., Testicular, Tanner Stage) #
- CBC, diff, plt #
- Urinalysis #
- Bone Marrow
- CSF
- Bili T/D #
- ALT #
- Serum amylase and/or lipase #
- Creatinine #
- Echocardiogram
- MRD Studies § (6-10 ml bone marrow)
- SNP Studies § (10 ml peripheral blood)
- Neuropsychological (NP) testing %
- Abd/Pelvic CT, Testicular Ultrasound**
- Testicular Biopsy**

Need to be done within 24 hours from starting induction therapy

§ For Minimal Residual Disease (MRD) and host somatic gene polymorphisms (SNP) **See Section 15.4 for specimen collection and shipping.**

% To be administered within 3 months of successful Induction following relapse and before initiating CRT. A follow-up study will be conducted at two years following completion of therapy on this study (+/- 3 months). See Section 16.0 for NP Battery.

** ITR patients only

TOXICITIES AND DOSAGE MODIFICATIONS:

See Section 5.0.

SPECIMEN REQUIREMENTS:

Required materials for Submission

Peripheral Blood for SNP studies: Submit 10 cc of peripheral blood in a purple top (EDTA) tube for polymorphism studies at study entry, prior to the start of Induction.

Bone marrow for MRD studies: Submit two aliquots (3-5 cc each) of BM in a tube with 2 mL of shipping media. One aliquot will be sent to the Flow Cytometry Lab at the University of Washington and one to the Molecular Lab at Columbus Children's.

See 15.4.1.1 for shipping information.

BIOLOGY REQUIREMENTS:

MRD testing, gene polymorphisms and neuropsychological testing is optional.

TREATMENT PLAN:

EXPERIMENTAL DESIGN SCHEMA

