

COG-ADVL04P2: A Feasibility Pilot and Phase 2 Study of Chemoimmunotherapy with Epratuzumab for Children with Relapsed CD22-Positive Acute Lymphoblastic Leukemia

FAST FACTS

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. Reservation Requirements

Investigators should refer to the COG website to determine if the study is currently open for accrual. If the study is listed as active, investigators should then access the Studies Requiring Reservations page to ensure that a reservation for the study is available. To access the Studies Requiring Reservations page:

- a. Log in to <https://members.childrensoncologygroup.org>.
 - b. From the menu bar, click **eRDES**. The *eRDES* sub-menu appears.
 - c. Click **Reservation**. The *Studies requiring Reservations* page appears.
2. All studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated below.
3. Patients must be ≥ 2 years and ≤ 31 years of age at the time of study entry.
4. Patients must have immunophenotypic confirmation of CD22 expression ($\geq 25\%$ expression).
5. Disease Status:
Enrollment on Part B will be limited to those with **first, early** marrow relapses, with or without associated extramedullary disease, occurring < 36 months from the time of initial diagnosis. See Appendix I for definitions.
6. Performance Level: Karnofsky $\geq 50\%$ for patients > 10 years of age and Lansky ≥ 50 for patients ≤ 10 years of age (See Appendix II).
7. Prior Therapy
- a. Patients who relapse while receiving standard ALL maintenance chemotherapy will not be required to have a waiting period before entry onto this study.
 - b. Patients who relapse when they are not receiving standard ALL maintenance therapy must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to entering this study.
 - Cytotoxic therapy: At least 14 days since the completion of cytotoxic therapy with the exception of hydroxyurea
 - Biologic (anti-neoplastic) agent: At least 7 days since the completion of therapy with a biologic agent. For agents that have known adverse events occurring beyond 7 days after administration, this period must be extended beyond the time during which adverse events are known to occur.
 - Stem Cell Transplant or Rescue: No evidence of active graft vs. host disease and ≥ 4 months must have elapsed.

8. Organ Function Requirements

- a. Patients must have adequate renal function defined as:
 - Creatinine clearance or radioisotope GFR $\geq 70\text{mL}/\text{min}/1.73\text{m}^2$ or
 - A serum creatinine based on age 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 34 utilizing child length and stature data published by the CDC.

- b. Patients must have adequate liver function defined as:
 - Bilirubin (sum of conjugated + unconjugated) \leq 1.5 x upper limit of normal (ULN) for age, and
 - SGPT (ALT) \leq 5 x upper limit of normal (ULN) for age, unless the elevation is disease-related
 - Serum albumin \geq 2 g/dL.
- c. Patients must have adequate cardiac function defined as:
 - Shortening fraction of \geq 27% by echocardiogram or
 - Ejection fraction of \geq 45% by gated radionuclide study
 - Cumulative prior anthracycline exposure of \leq 400 mg/m² (each 10 mg/m² of idarubicin should be calculated as the isotoxic equivalent of 30 mg/m² of daunorubicin or adriamycin).
- d. Patients must have adequate pulmonary function defined as:
 - No evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry $>$ 94% if there is clinical indication for determination.

EXCLUSION CRITERIA:

1. Pregnancy or Breast-Feeding
There is yet no available information regarding human fetal or teratogenic toxicities. Pregnancy tests with a negative result must be obtained in girls who are post-menarcheal. Males or females with reproductive potential may not participate unless they have agreed to use an effective contraceptive method. Women may not breast-feed while on protocol therapy.
2. Patients with Down syndrome are excluded due to the administration of methotrexate in Block 2.
3. Patients with B-cell ALL (L3 morphology or evidence of *myc* translocation by molecular or cytogenetic technique) are not eligible.
4. Patients with documented active and uncontrolled infection at time of study entry are not eligible.
5. Patients who are currently receiving another investigational drug are not eligible.

REQUIRED OBSERVATIONS:Required observations and Optional Research Studies Pre-Study

All entry/eligibility studies must be performed within 1 week prior to study entry (unless otherwise specified).

STUDIES TO BE OBTAINED Pre-Study

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| 1. History | 10. Chest x-ray |
| 2. Physical Exam with vital signs | 11. Echocardiogram or gated radionuclide study |
| 3. Height, weight, BSA | 12. Prothrombin, partial thromboplastin time and fibrinogen |
| 4. Performance Status | 13. Bone marrow for MRD (Section 8.3.2) (required) |
| 5. CBC, differential, platelets | 14. Lumbar puncture with CSF cell count and cytospin cytology. |
| 6. Urinalysis | 15. Pregnancy Test ¹ |
| 7. Electrolytes including glucose, Ca ⁺⁺ , PO ₄ , Mg ⁺⁺ | 16. Correlative Biology Studies ² (Section 8.2) |
| 8. Creatinine, SGPT, bilirubin | |
| 9. Total protein/albumin | |

¹ Patients of childbearing potential require a negative pregnancy test prior to starting treatment and must use an acceptable method of birth control. Abstinence is an acceptable method of birth control.

² See Section 8.2 for specifics of optional correlative biology studies in consenting patients.

TREATMENT PLAN:

Patients will receive 4 weekly doses of Epratuzumab during Block 1 of therapy. After completion of Block 1, patients will proceed on to Block 2 and Block 3 chemotherapy, which are identical to the blocks used in the AALL01P2 study for first early and late marrow relapse.

SPECIMEN REQUIREMENTS:

Two (2) mL of bone marrow will be collected pre-study and Day 36 of each Block of chemotherapy for determination of MRD. The pre-study and Day 36 Block 1 samples are required, as MRD at the end of Block 1 is a study endpoint. End of Block 2 and 3 samples are optional and should be submitted in consenting patients.

See Appendices VI and VII for Sample Collection Procedures and Shipping Addresses for MRD studies

.For more information on this protocol, contact GRCOP at 616.391.1230.