

SWOG S0805: Phase II Study of Combination of Hyper-CVAD and Dasatinib (NSC-732517) with or without Allogeneic Stem Cell Transplant in Patients with Philadelphia (Ph) Chromosome Positive and/or BCR-ABL Positive Acute Lymphoblastic Leukemia (ALL) (a BMT Study)

Fast Facts

Dasatinib provided.

INDUCTION/CONSOLIDATION REGISTRATION (Registration Step 1):

1. Patients must have a morphologic diagnosis of acute lymphoblastic leukemia (ALL), as defined in Section 4.1b, with evidence of ALL involvement in bone marrow and/or blood. Patients with only extramedullary disease in the absence of bone marrow or blood involvement are not eligible. Patients with M0 AML or mixed lineage leukemia are not eligible for this study. Patients with L3 (Burkitts) are also not eligible.
 - a. For ALL in marrow or peripheral blood, immunophenotyping of the blood or marrow lymphoblasts must be performed to determine lineage (B cell, T-cell, or mixed B/T cell). NOTE: Appropriate marker studies including CD19 (B cell), CD10, CD5, and CD7 (T cell) must be performed. Coexpression of myeloid antigens (CD13 and CD33) will not exclude patients. If possible, the lineage specific markers cytoplasmic CD22 or CD79a (B cells), cytoplasmic CD3 (T cells) and cytoplasmic MPO (myeloid cells) must be determined.
2. Patients may have received no more than one course of remission induction therapy for ALL, providing this induction course was given prior to the results of the cytogenetics testing for Ph/BCR/ABL status being known. Patients who have received any post-remission therapy for ALL or who have relapsed from complete remission are not eligible. (Patients with previously untreated ALL can be eligible, and patients who have received one course of remission induction therapy for ALL can be eligible, regardless of their response to therapy.) Any prior induction chemotherapy must have been completed within 28 days prior to registration.
3. For patients who have received any prior therapy that was NOT remission induction therapy, one of the following must be true:
 - a. At least 6 weeks must have elapsed since any monoclonal antibodies were given, at least 7 days must have elapsed since any other treatment was given, and all toxicities of the remission induction therapy must have resolved to Grade ≤ 2 ; or
 - b. The patient must have rapidly progressive disease (per institutional guidelines).
4. For previously treated patients, the Study Coordinator must be contacted before registration, in order to determine the regimen to be given in the first course of induction/consolidation therapy, based on prior therapy.
5. Patients must be Philadelphia (Ph) chromosome positive and/or BCR/ABL positive as confirmed by standard cytogenetics, FISH, and/or polymerase chain reaction (PCR) testing performed by local laboratory. NOTE: Samples will be submitted centrally for verification of results (see Section 5.1n).
6. Patients must have a bilirubin $\leq 3.0 \times$ Institutional Upper Limit of Normal (IULN) within 14 days prior to registration.
7. Patients must have SGOT (AST) $\leq 3.0 \times$ IULN and/or SGPT (ALT) $\leq 3.0 \times$ IULN within 14 days prior to registration. If both tests are done then both values must be $\leq 3.0 \times$ IULN.
8. Patients must have a serum creatinine $\leq 3.0 \times$ IULN within 14 days prior to registration.
9. Patients must not have active pericardial effusion, ascites, or pleural effusion of any grade, or prolonged QTc interval (QTc > 480 msec).
10. Patients must have Zubrod Performance Status of 0-2.
11. Patients must be ≥ 18 and ≤ 50 years of age.
12. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.
13. Patients must be registered on SWOG-9007 ("Cytogenetic Studies in Leukemia Patients"). Collection of pretreatment marrow specimens must be completed within 28 days prior to registration. Pretreatment specimens of bone marrow (or peripheral blood if the marrow aspirate is a dry tap) must be submitted to an approved Southwest Oncology Group Cytogenetics Laboratory for cytogenetics analysis. Note that protocol SWOG-9007 also requires submission of remission and relapse specimens.
14. Patients must be registered on S9910 ("Leukemia Centralized Reference Laboratories and Tissue Repositories Ancillary"). Collection of pretreatment blood and/or marrow specimens must be completed within 28 days prior to registration. Pretreatment specimens of marrow and/or peripheral blood must be submitted to the Southwest Oncology Group Lymphoid Leukemia Repository in Seattle, Washington for cellular and molecular studies,

including verification of BCR/ABL status (see Section 7.8a). Note that protocol S9910 also requires submission of follow-up specimens.

15. Patients must not be pregnant or nursing because of the teratogenic potential of the drugs used in this study. Women/men of reproductive potential must have agreed to use an effective contraceptive method. Women of reproductive potential must have a negative pregnancy test performed within 14 days prior to registration.
16. Patients must not have prior history of known Type I hypersensitivity or anaphylactic reactions to doxorubicin.
17. All patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
18. At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered into the data base.

Pre-Study Parameters

1. History and Physical Exam, Weight and PS
2. Baseline Abnormalities
3. CBC, Differential, Platelets, Total Bilirubin, SGOT and/or SGPT, Serum Creatinine
4. Uric Acid
5. Bone Marrow Aspirate/Biopsy
6. Pregnancy Test
7. Biopsy for Testicular Involvement if clinical findings are equilateral
8. FISH and/or PCR to confirm Ph(+) and/or bcr- abl+
9. Chest X-Ray
10. Echo/MUGA

Treatment

SCHEMA

