91-038

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To: SGHM
SGI
In Turn

From: SGHMCO

Subj: Treatment Summary, Protocol SWOG 8954

1. TITLE: Evaluation of the L-17M Protocol in the Management of Patients with Lymphoblastic Lymphoma, Phase II, Pilot

2. BACKGROUND: Lymphoblastic lymphoma (LL) is a distinct subgroup among diffuse poorly differentiated lymphocytic lymphomas. Clinical features of the disease include: 1) frequent occurrence in children and adolescents, 2) presentation with a mediastinal mass in about 50% of cases, 3) presentation with extranodal disease in the absence of a mediastinal mass in about 50% of cases, 4) high incidence of bone marrow and peripheral blood involvement, 5) clearly recognizable immaturity of the neoplastic cells, 6) increased incidence in males relative to females, 7) the presence of T cell markers on the malignant lymphocytes.

The distinction between LL and T cell acute lymphocytic leukemia (T-ALL) is often difficult to determine. Clinically, the two diseases are distinguished by the degree of bone marrow involvement at the time of diagnosis. Although T-ALL and LL appear to be one disease, they are different disease entities corresponding to malignant proliferation of immature T lymphocytes at different stages of maturation.

While the precise phenotypic characteristics of LL are unknown and while the clinical distinction from ALL may not always be clear, it is generally accepted that conventional therapeutic approaches used in other non-Hodgkin's lymphomas are inadequate for the treatment of LL. In addition, there has been relatively little reported in the literature regarding the treatment of adult patients with LL.

Because of the similarity between LL and ALL, adult patients with LL have been treated on various ALL protocols at Memorial Sloan Kettering Cancer Institute (MSKCC). All patients were previously untreated and, for the purpose of analysis, were divided into leukemic and non-leukemic subgroups. The composite CR rates for the non-leukemic and leukemic LL patients on all protocols were 80% and 77% respectively. While there was no difference in CR between the earlier vs. the later protocols, there was an improvement in overall survival when patients on the early vs. the later protocols were compared.

MSKCC protocols have been used extensively by the Southwest Oncology Group members in the treatment of adult patients with acute lymphoblastic leukemia. Because of the results obtained at MSKCC in the treatment of LL and because of SWOG's familiarity with these protocols, the L17M protocol will be used in this Phase II study.

The objectives of this study are: 1) to assess the response rate and response duration of LL treated with the L-17M protocol; 2) to assess the qualitative and quantitative toxicities of the L-17M protocol administered in a Phase II study; 3) to assess the immunophenotypic characteristics of adult lymphoblastic lymphoma.

3. BIBLIOGRAPHY: The bibliography for the studies sited as well as for the entire protocol is found in Section 18.0 on page 40 of the protocol.

4. TECHNICAL APPROACH: Eligible patients will be those with biopsy proven lymphoblastic lymphoma. Patients cannot have received prior chemotherapy or radiation. All patients must have a performance status of 0-2 and adequate renal and hepatic function. Patients must be 15 years of age or older. Patients cannot have a history of impaired cardiac status. Patients with AIDS or HIV associated complex are ineligible. Pregnant or lactating women may nor participate in this study. Patients of reproductive potential must agree to use effective contraception. No prior malignancy is allowed except for adequately treated basal or squamous cell skin cancer, in situ cervical cancer or other cancer for which the patient has been disease-free for five years.

The treatment plan is quite extensive. All patients will receive the same induction and therapy. If patients remain eligible, they will also receive consolidation and maintenance therapy. Tables summarizing induction, consolidation and maintenance treatment plans are attached at the end of this summary.

5. EQUIPMENT: Conventional laboratory and clinical equipment and drugs will be utilized.

6. INVESTIGATIONAL SCHEDULE: This study will begin as soon as approved by the IRB and signed by the Commander. A total of 50 eligible patients will be accrued to this study, at which time accrual will be permanently discontinued. Fifty patients are sufficient to estimate the complete response probability or the probability of a particular toxicity. In addition, time to treatment failure and survival will be investigated. The Southwest Oncology Group expects to accrue 25 patients per year based on previous studies.

7. EXPERIMENTAL SUBJECTS: Compliance with Air Force Regulation 169-6 and Medical Center Regulation 169-1 will be carried out.

8. USE OF DRUGS: All FDA and NCI requirements will be followed.

9. PERSONNEL DATA:
Facility Commander: [redacted], Colonel, USAF, MC
Principal Investigator: [redacted], Lt Col, USAF, MC
Investigator: [redacted], Major, USAF, MC
Data Manager: [redacted]