

1.0 BACKGROUND

Because of proximity to the shipyards during World War II, a number of CALGB institutions are treating a relatively large number of patients. Series from the Massachusetts General Hospital (1), the DFCI (2), and Mount Sinai (3), have been reported recently.

The median survival after diagnosis of patients with malignant mesothelioma in most series ranges between five and twelve months (1-6). Most patients with mesothelioma die of local complications of primary disease and not of distant metastases; therefore, a greater emphasis on achieving local control seems indicated.

A small percentage of selected patients at a number of institutions who have undergone subtotal surgical resection, followed by radiotherapy and chemotherapy, have achieved a five-year disease-free survival (7-10). Of 66 patients seen at Memorial Hospital, 54 were explored and 33 resected (28 pleurectomies and 5 pleuropneumonectomies). Of the 33 resected patients, 7 were disease-free at 17 to 69 months (median 24). In addition, 5 relapsed but survived five years or more (9).

Of 11 patients treated by radical extrapleural pneumonectomy by the Chicago group, there were 2 disease-free survivors at 2 and 4 years (8). A third study, from England, reported 29 patients radically resected; two of these are disease-free at 3.5 and 6 years (7). While neither of the first two studies reported any operative mortality, an unacceptable hospital mortality of 31% was observed in the third (a percentage which the authors felt could be decreased considerably by better patient selection) (7). In addition to disease-free survivors, resection resulted in a longer median survival (compared to patients treated with radiotherapy and/or chemotherapy alone), and decreased morbidity from chest pain and recurrent pleural effusions. The most effective treatment for diffuse mesothelioma has not been established.

ECOG, SWOG, and SECSG are currently undertaking a study of primary radiotherapy, with patients then randomized to receive Adriamycin or no further therapy. Chemotherapy of mesotheliomas has been reviewed recently by Aisner (11). Adriamycin and cyclophosphamide appear effective in approximately one in three patients (2); the efficacy of DTIC is being assessed by the Southwest Oncology Group. The activity of most standard single agents in this disease is unknown. Active agents or combinations are obviously required.

2.0 OBJECTIVES: This protocol outlines the procedure for Phase II studies to evaluate the efficacy of intensive treatment of patients with histologically proven malignant mesothelioma.

activity will be determined by the frequency of complete or partial remission. The duration of response, survival, and the quality of survival will be balanced against toxicity as provided by clinical and laboratory data.

3.0 ELIGIBILITY CRITERIA: Patients must fulfill the following criteria for eligibility:

3.1 Histologically confirmed malignant mesothelioma: Epithelial, Sarcomatoid, or Mixed.

3.2 Measurable or Evaluable Disease

3.21 Measurable disease: Any mass reproducibly measurable in two perpendicular diameters by X-ray, nucleotide scan, computed tomography, or ultrasonogram (USG).

3.211 A previously irradiated lesion after documented disease progression.

3.212 Hepatic disease: A clearly defined mass on liver scan, ultrasound or computerized tomographic (CT) scan considered to represent metastatic disease; or histologically documented hepatic metastasis with an enlarged liver >5 cm. below the costal margin.

3.22 Evaluable Disease: Lesions apparent on chest x-ray, CT, or USG which do not fit the criteria for measurability. Patients with both measurable and evaluable disease will be evaluated by criteria for measurable disease.

3.221 Ill-defined post surgical masses,

3.222 Diffuse parenchymal malignant disease,

3.223 One dimensional mediastinal or hilar adenopathy.

3.224 Pleural lesions measurable in one dimension only.

3.23 Pleural or peritoneal effusions are neither measurable nor evaluable.

3.3 Performance score 0-2 (<50% of waking hours in bed).
Life expectancy >2 months.
Adequate nutrition (>1000 cal).

3.4 Prior Treatment:

>2 weeks since surgery.

No prior chemotherapy

>4 weeks since prior RT:

2 wks if measurements document progression, and toxicity resolved from prior RT. Detail on flow sheets