#681

THE FRED HUTCHINSON CANCER RESEARCH CENTER
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DEPARTMENT OF MEDICINE, DIVISION OF ONCOLOGY
(10/11/91)

1. Busulfan and Cyclophosphamide Conditioning for Autologous Transplantation for Patients with Metastatic Breast Cancer

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2. Introduction

This protocol replaces protocol #329.2 which currently uses busulfan (BU) + cyclophosphamide (CY) in a dose escalation, toxicity trial plus CD34 selected autologous marrow for the treatment of patients with advanced breast cancer. Changes are proposed in order to have an "all inclusive" treatment protocol for patients with breast cancer receiving BU/CY.

The proposed changes are to alter the BU + CY dose escalation schema so that the next higher dose levels will increase the doses of BU rather than increasing the CY as in the old schema. In addition, patients will all receive anti-TNF therapy similar to protocol #654 (recently reviewed by the CIC). Preliminary results of autologous marrow transplantation for breast cancer using BU and CY indicate promising anti-cancer activity with 4/8 evaluable patients who had stage IV disease achieving a complete response. This protocol is designed to determine the maximum tolerated doses of the Bu + Cy regimen when used with drugs that inhibit tumor necrosis factor (TNF-α). The sources of marrow have changed from only CD34 selected marrow to CD34 selected marrow, untreated marrow or G-CSF stimulated peripheral blood mononuclear cells (protocol #656). Patients who do not have adequate numbers of marrow cells harvested for treatment or who cannot have marrow stored can thus be treated on this dose escalation study.

Background

A. Conditioning Regimen.

Combination chemotherapy has been employed as the major means of treatment for patients with both recurrent or disseminated estrogen receptor (ER) negative breast carcinoma, as well as estrogen receptor positive carcinoma which has become refractory to hormonal manipulation. The response rate of ER-negative metastatic breast carcinoma (MBC) to chemotherapy regimens incorporating Adriamycin is 70 to 80% and a complete response occurs in 15 to 20% of such patients (1,2). The overall response rate of ER-positive MBC is on the order of 50 to 60% (3). However, the survival of these patients remains poor and essentially all patients eventually die of MBC. The respective median survival from initial recurrence is 12 to 18 months for ER-negative and about 30 months for ER-positive disease, with expected 5-year survivals of <5% and