

## **Correlation between her-2 Neu overexpression and response to high dose paclitaxel in Stage IV breast cancer- a retrospective study**

### **A. Study purpose and rationale**

Overexpression of her-2neu has been found in approximately 20-30% of breast cancer. It is associated with reduced overall survival time as well as time to relapse. Multiple Phase II trials have shown that a single cycle of high dose chemotherapy can produce disease free survivals of 15-20% for at least three years and that a complete response is the most significant factor in prolonging disease free survival. One strategy in the attempt to increase the complete response rate has been sequential cycles of high dose chemotherapy. Paclitaxel, with its 60-70% response rate even at conventional doses, has become a common agent incorporated into these regimens. However, there are nonresponders and prior studies have shown that her-2neu overexpression confers increased resistance to paclitaxel. It would be of great interest to identify whether this is the basis for lack of clinical response in those patients who do not respond to paclitaxel containing regimens. Given the side effects, especially that of peripheral neuropathy, it would be useful to identify/predict those patients who would benefit the most. A pilot study of 37 patients with responding Stage IV breast cancer treated with three cycles of high dose chemotherapy, including paclitaxel showed no correlation between survival and her-2neu overexpression. However, it is the feeling that larger population is needed to establish this relationship. The latter is the goal of this study.

### **B. Study design and statistical analysis**

The study will be a retrospective analysis of patients with responding Stage IV breast cancer who had undergone high dose chemotherapy (HDC) with sequential Taxol, melaphan and Cyclophosphamide. Pre-treatment tumors were immunohistochemically stained with mouse monoclonal antibody against her-2neu. Slides stained institutions outside of CPMC will be brought here for restaining. In addition, slides stained prior to 1996 will also be restained. Post HDC response will be looked at in terms of being positive (i.e both complete and partial response) and no response (stable disease and progression of disease). Data will then be analyzed with regard to her-2neu status and clinical response to therapy.

### **C. Study procedures|Drugs|Medical Devices|Study questionnaires:**

None

### **D. Study Subjects**

Two hundred subjects will be looked at in this study. This number gives the 4-power to detect at least a 20% clinically significant difference  $\{8(n=p_1q_1 + p_2q_2)/\Delta + 2/\Delta\}$ . Subjects are to be obtained from a database of patients who have undergone high dose chemotherapy with sequential Taxol, melaphan and CTcB. These were women aged 18-60 with responding stage IV breast cancer. A complete response (CR) was defined as the disappearance or a >50% reduction in the sum of the products of the largest perpendicular diameter of all measurable disease for four weeks. Partial response (PR) was defined as complete resolution of all soft tissue or visceral disease with sclerosis of prior lytic bone lesions. Stable disease was defined as a <25% reduction in the bidimensional measurements of the lesions. Disease progression was defined as increase of at least 25% in tumor size or new lesions. Patients were required to have adequate to normal cardiac and liver function as well as performance status based on a

standard scale. Patients with CNS metastases, progression of disease while on prior taxane therapy, pre-existing neuropathy and prior mitomycin C & cisplatin therapy were excluded from the study.

**E. Recruitment of Subjects:**

Old charts as well as database

**F. Potential Risk to subjects/Potential conflict of interest:**

None

**G. Potential Benefit:**

Identification of patients best suited for high dose Taxol therapy

**H. Compensation or cost to subjects/radiation or radioactive substances:**

None