

ADVANCES IN BREAST CANCER

by: Gil Lederman, MD

One of the most important oncology research papers this year deals with breast cancer treatment.

Over the years, studies have shown that adjuvant or additional chemotherapy - or hormonal therapy - improves outcome in selected patients with breast cancer. These studies have encouraged oncologists to recommend in appropriate circumstances these therapies after surgery for women diagnosed with breast cancer.

Other studies have shown that removal of the lump of cancer (lumpectomy) followed by radiation results in outcome equal to mastectomy - meaning that mastectomy for most women with breast cancer is not necessary and serves no additional purpose. Of course, it is used when the breast cannot be saved or when the involved parties have no motivation for preservation.

In select cases, mastectomy is used. The most appropriate cases for mastectomy is that of diffuse disease in the breast - that is, disease that is not confined to a specific area.

Researchers led by Overgaard et al from the Danish Breast Cancer Cooperative Group published in a recent New England Journal of Medicine the results of a study geared to determine whether radiation given to those having undergone mastectomy and chemotherapy resulted in improvement in outcome.

Selected for study included women with breast cancer involving at least one high risk feature.

What were considered high risk features? Lymph node involvement with cancer, cancer measuring 5 centimeters (approximately two inches in the breast), invasion of the skin or muscle underneath the breast as well as no evidence of cancer spread beyond the local area. All women underwent testing to confirm that the cancer did not spread beyond the breast or local lymph nodes.

Patients were evaluated between 1982 and 1989 and were randomly assigned to have chemotherapy plus radiation, chemotherapy alone or chemotherapy plus hormonal therapy. The chemotherapy plus hormonal therapy arm was stopped because of a high mortality rate.

Chemotherapy used for patients included Cyclophosphamide, Methotrexate and Fluorouracil (CMF) which was administered intravenously every four weeks.

Women who were to get radiation plus chemotherapy commenced the radiation one week after the first chemotherapy treatment and thereafter completed the radiation before recommencing chemotherapy.

This was a major study involving 1789 women. Because of some ineligibilities within the group upon re-examination, 1708 pre-menopausal women were randomized including 852 to radiation plus chemotherapy and 856 to chemotherapy alone. At time of analysis, with an average follow up of nearly ten years, the cancer had recurred in 858 patients, with 842 having died.

The authors noted, "The probability of disease-free survival was significantly higher in the group that received radiotherapy plus CMF (combination chemotherapy) than in the group treated only with CMF." Furthermore, the authors noted, "Locoregional recurrence was significantly more frequent in the group treated with CMF alone."

At ten years, 54% of women alive if they had undergone chemotherapy and radiation compared to 45% with chemotherapy alone.

Furthermore, locoregional recurrence was noted in 80% of women treated with chemotherapy alone. The authors stated that "The addition of radiation to chemotherapy reduced the frequency of locoregional recurrence to about one-fourth that found in the groups that did not receive radiotherapy."

Features of the cancer at increased risk for locoregional recurrence included the size of the primary breast cancer, the number of lymph nodes containing metastatic cancer the degree of aggressiveness of the cancer as determined pathologically or under the microscope by the pathologist examining the cancer.

It is clear that "results indicate that the addition of radiotherapy to adjuvant chemotherapy after total mastectomy and axillary dissection reduces locoregional recurrences and improves survival."

Women whose breast cancer occurs in the chest wall after mastectomy often have a very difficult situation controlling this tumor. It is difficult to maintain hygiene. These tumors not infrequently bleed.

The authors noted "The problem of local recurrence is not related solely to the management of the axilla, since more than half the recurrences were on the chest wall. Recurrences on the chest wall and axilla (without concomitant distant metastases) were treated with curative intent. Most patients who did not receive radiotherapy were treated with resection of the recurrent tumor followed by radiotherapy, whereas patients who had received radiotherapy were treated with surgery alone. The significant difference in overall survival between the group treated with radiotherapy plus CMF and the group given CMF alone indicates that second-line treatment cannot compensate for inadequate primary therapy."

The authors concluded, "Our study strongly indicates that optimal results of the treatment of high risk breast cancer can be achieved only by controlling both locoregional and systemic tumors. With current surgical methods of treatment, radiotherapy seems required for adequate locoregional control in high risk premenopausal patients."

This important work will continue to guide patients, surgeons and oncologists about recommendations for the best care - even after mastectomy is performed.