

POTENTIAL BENEFITS OF CHEMOTHERAPY FOR BREAST CANCER PATIENTS

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One of the most important combination chemotherapeutic regimens used for those with breast cancer is nicknamed CMF. It stands for Cyclophosphamide, Methotrexate and Fluorouracil.

It was innovative treatment initially proposed twenty years ago by Gianni Bonadonna et al from the National Cancer Institute of Italy. Now published as the lead article in the New England Journal of Medicine is the twenty year follow up of the women randomly allocated to receive CMF chemotherapy for twelve monthly cycles compared to no systemic treatment.

A randomized study is best equipped to answer the question "Does treatment alter outcome?" This has been a highly respected study and informed women of equal prognostic groups received combination chemotherapy or not. The twenty years' results evaluate potential benefits as well as toxicities.

This study consisted of women aged 75 years or younger with pathologic confirmation of breast cancer involving at least one axillary node. Patients were evaluated by age and number of lymph nodes involved. Between 1973 and 1975, 391 patients entered the study. Treatment failure was called if the disease recurred.

The researchers evaluated relapse-free survival - meaning no evidence of recurrent breast cancer - and as well, overall survival. Patients treated with adjuvant chemotherapy fared better in both categories than those who were treated with surgery alone. The median time to relapse was 40 months in the control group compared to 83 months in the group receiving CMF. Survival was greater in those women receiving chemotherapy - 137 months compared to 104 months.

The authors noted that while recurrences most commonly occurred in the first three years after diagnosis, the divergence of survival curves was noted only after the 7th year. Survival after relapse was similar in both groups. This would suggest that subsequent chemotherapeutic and other treatments had a similar palliative effect on patients with recurrence.

Post menopausal women and patients with four to ten positive lymph nodes did not evidence a benefit from receiving the combination chemotherapy.

The authors noted "The greatest benefit of CMF treatment was among patients with one to three positive nodes." Interestingly, of nine women who had more than ten positive nodes and received no combination chemotherapy, none were alive twenty years later compared to three of eighteen patients who had received CMF chemotherapy and were alive twenty years later.

Furthermore, statistical analysis showed "The number of involved lymph nodes remained the most important prognostic factor followed by the type of treatment with adjuvant chemotherapy." The authors noted "The main therapeutic effect of adjuvant CMF was to reduce the incidence of distant metastases."

The authors attempted to explain why post menopausal women did not benefit from chemotherapy like pre-menopausal women. Some suggested that the only benefit of chemotherapy was to ablate the ovaries thereby eliminating this source of hormone production. Others proposed that older women received lower doses of chemotherapy, therefore, yielding a lesser benefit.

What is remarkable is the fact that at 20 years, patients still have an improved relapse-free survival - that means being free of cancer as well as being as being alive - in groups having been treated with this combination chemotherapy regimen.

Some women fear that the diagnosis of cancer means death. This study obviously shows that many women - in fact, at 20 years - there was more than a 30% probability of being alive, free of cancer. The potential advantage of receiving chemotherapy early on is to remain free of cancer. However, it should be noted that there was, as well, a group of women alive with cancer twenty years after the diagnosis was made.

The authors noted "The main therapeutic effect of adjuvant CMF was to reduce the incidence of distant metastases (ten percentage point difference at twenty years between patients who received CMF and those that did not)."

Craig Henderson, formerly the Director of the Breast Evaluation Clinic at the Harvard Medical School, Dana Farber Cancer Institute, and presently at the University of California San Francisco, in an editorial notes, "The results of adjuvant chemotherapy have been confirmed in additional studies and in an overview of all adjuvant studies. The report by Bonadonna and his colleagues demonstrates that the effects are lasting."

Certainly, there have been many great strides taken since this study was commenced twenty-two years ago. They occurred on the shoulders of giants.