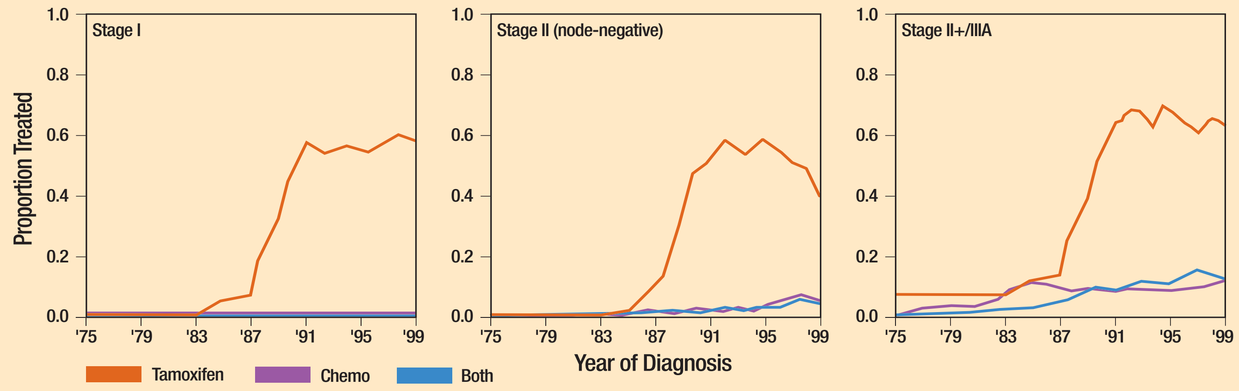
CALGB 49907: Adjuvant Chemotherapy in Elderly Women

25TH ANNUAL San Antonio Breast Cancer Symposium 17

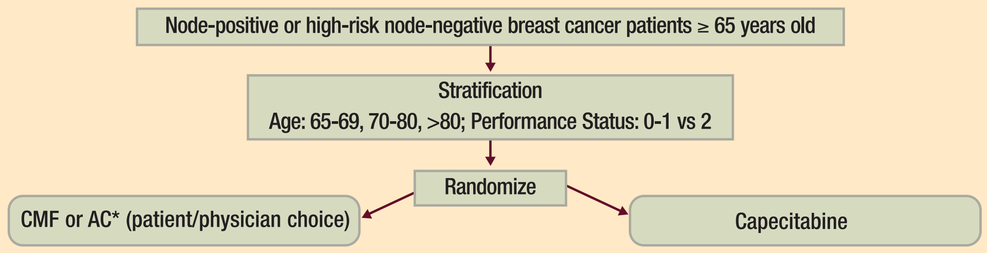
Recent patterns of care data suggest that while adjuvant endocrine therapy is commonly utilized in elderly women, chemotherapy is infrequently administered. A major related factor is that relatively few randomized trials of adjuvant chemotherapy have included elderly women, so there is a paucity of data on risks and benefits. This is particularly problematic in higher risk older women with estrogen receptor-negative tumors. An intriguing new trial has just been launched to address this important issue. CALGB 49907 randomizes elderly women with primary breast cancer to either capecitabine or combination chemotherapy. An innovative partnership with the Y-ME National Breast Cancer Organization has been developed to assist in educating patients about the study.

ADJUVANT SYSTEMIC THERAPY: WOMEN OVER AGE 69



Adapted from Mariotto A et al. *J Natl Cancer Inst* 2002;94(21):1626-1634.

CALGB 49907: A RANDOMIZED TRIAL OF ADJUVANT CHEMOTHERAPY WITH STANDARD REGIMENS (CMF OR AC) VERSUS CAPECITABINE IN WOMEN 65 YEARS AND OLDER WITH NODE-POSITIVE OR HIGH-RISK NODE-NEGATIVE BREAST CANCER



*** Patients whose LVEF is not within lower limits of normal must receive CMF, not AC.**
All ER/PR+ patients receive tamoxifen x 5 years.
Source: CALGB 49907 Protocol.

CALGB 49907: QUALITY OF LIFE SUBPROTOCOL

Primary Objective: Compare the quality of life in terms of physical, cognitive, social and emotional functioning.

Hypothesis A: Patients treated with capecitabine will have significantly fewer physical symptoms and consequently better emotional state, with less time traded off to obtain normal health than patients treated by either CMF or AC.

Secondary Objective: Evaluate the influence of other sociodemographic, medical and psychosocial variables on older patients' adjustment and overall quality of life.

Hypothesis B: Older women most vulnerable to the stresses of breast cancer, exhibiting the greatest distress, are those with worse comorbid conditions, poorly managed chemotherapy side effects, worse physical functioning at study entry, fewer socioeconomic resources, more stressful life events, inadequate social support, and no psychosocial services.

Source: CALGB 49907 Protocol.

PEER-BASED COUNSELING: CALGB & Y-ME JOIN FORCES TO ASSIST PATIENTS

Y-ME National Breast Cancer Hotline
1-800-221-2141 (English)
1-800-986-9505 (Español)

Y-me National Breast Cancer Organization

"Patients who are undecided about participation in this trial will be offered the opportunity to speak with a volunteer counselor from the Y-ME National Breast Cancer Organization. This optional 'peer-based' counseling will provide general information about clinical trials, details about this clinical trial and emotional support."

Source: CTSU and Y-ME websites.

SELECT PUBLICATIONS

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Adams J et al. **Recruiting older adults for clinical trials.** *Control Clin Trials* 1997;18(1):14-26.

Comis R, Kelaban A. **Enhancing cancer care and clinical trials: New paradigms for success.** *Cancer Control* 1997;4(5):430-433.

Ellis PM. **Attitudes towards and participation in randomised clinical trials in oncology: A review of the literature.** *Ann Oncol* 2000;11(8):939-945.

Ellis PM et al. **Randomized clinical trials in oncology: Understanding and attitudes predict willingness to participate.** *J Clin Oncol* 2001;19:3554-3561.

Hutchins LF et al. **Underrepresentation of patients 65 years of age or older in cancer-treatment trials.** *N Engl J Med* 1999;341(27):2061-2067.

Klabunde CN et al. **Factors influencing enrollment in clinical trials for cancer treatment.** *South Med J* 1999;92(12):1189-1193.

O'Shaughnessy JA. **Potential of capecitabine as first-line therapy for metastatic breast cancer: Dosing recommendations in patients with diminished renal function.** *Ann Oncol* 2002;13(6):983.

INTERGROUP TRIAL OF ADJUVANT CHEMOTHERAPY IN OLDER WOMEN

We are launching a trial for women age 65 and older who have either node-positive or high-risk, node-negative breast cancer. Patients will be randomized to either capecitabine or standard therapy with either CMF or CA. This trial will determine if oral capecitabine for six courses is equivalent to either CMF or CA, with perhaps less toxicity.

Quality of life and the influence of comorbidity on outcome will also be studied, as will the functional status of the patients. We're very excited about this, because we believe that if capecitabine is equivalent to more intensive regimens, it might be very attractive for many patients as an adjuvant regimen. I believe that a lot of physicians will be willing to put patients on this trial. The patients are there, and I feel confident we will meet accrual.

If you look at Phase II trials in metastatic breast cancer as second- and third-line therapies, there is now a reasonable database for capecitabine demonstrating response rates of about 20% to 30%, which really is comparable to taxanes, vinorelbine and other very active agents.

There is also a very small comparison of capecitabine versus CMF in metastatic disease where the response rate was higher, although not significantly, for capecitabine. So, if you look at capecitabine as a single agent, it fits in.

—Hyman Muss, MD

QUALITY-OF-LIFE ASSESSMENT

"Given that 60% of all cancer patients are 65 years or older, and the paucity of information currently available on elderly cancer patients, there is a necessity for testing the efficacy of treatment regimens and their impact on quality of life in this patient population. For treatments that may only be marginally different with respect to survival, but significantly different in their side effects or their impact upon a patient's quality of life, quality of life becomes a major consideration in treatment choice. CMF or AC vs. capecitabine represents a test of this very issue. If capecitabine is determined to be significantly less toxic than CMF and AC and equally effective, this study would document the extent of improvement in elderly patients' quality of life related to a less toxic regimen. If capecitabine should prove not to be as effective as CMF or AC although less toxic, then a quality of life assessment assumes greater importance, with benefits of less toxicity offset by reduced efficacy."

—CALGB 49907 Protocol

TREATING THE ELDERLY WITH CYTOTOXIC CHEMOTHERAPY: FINDING A LESS TOXIC REGIMEN

The elderly is a group of patients that many physicians have been somewhat hesitant to treat aggressively with chemotherapy, because the benefit, although statistically significant, is small in this patient population. Europeans have been very strong in using hormonal therapy instead of cytotoxics in this population. We're looking for a more gentle, but reasonably active, drug combination or, in the case of capecitabine, a single drug.

It is interesting to look at capecitabine as an adjuvant treatment in an elderly population, where the options currently available, such as CMF, are rather toxic. Knowing that capecitabine has activity at least equivalent to CMF in advanced disease, may offer a minimally toxic regimen with benefit in a population of patients that we all are somewhat reticent to treat.

—Daniel Budman, MD