Breast Cancer Clinical Trials in Elderly Women

25TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM 23

A gradual shift in international demographics is resulting in an increasing number of elderly breast cancer patients, and this trend will accelerate with the aging of "baby boomers." A critical factor in clinical research in the elderly is the impact of comorbidity on noncancer mortality and the side effects and toxicity of antitumor therapy. Unfortunately, older women have been under-represented in cancer clinical trials, and very few studies have specifically focused on these patients. A recently activated groundbreaking CALGB randomized Phase III adjuvant study will randomize women over age 65 to either capecitabine or CMF/CA in an attempt to define a less toxic and more convenient adjuvant regimen.

PHASE III RANDOMIZED STUDY OF ADJUVANT CHEMOTHERAPY COMPRISING STANDARD CYCLOPHOSPHAMIDE, METHOTREXATE, AND FLUOROURACIL (CMF) OR DOXORUBICIN AND CYCLOPHOSPHAMIDE (AC) VERSUS ORAL CAPECITABINE IN ELDERLY WOMEN WITH OPERABLE ADENOCARCINOMA OF THE BREAST

Open Protocol

Protocol IDs: CLB-49907, CTSU
Projected Accrual: 600-1,800 patients

Eligibility	Breast cancer patients ≥ 65 years old, node-positive or high-risk node-negative
ARM 1	Standard therapy (CMF q4w x 6 or AC q3w x 4). Patients with insufficient LVEF receive CMF, patients with normal LVEF receive CMF or AC at physician's discretion
ARM 2	Capecitabine BID qd, days 1-14, q3w x 6

Beginning within 12 weeks after treatment in either arm, patients with ER- or PR-positive disease receive tamoxifen qd x 5 years. Beginning 4-6 weeks after treatment in either arm, eligible patients who previously underwent BCT undergo radiotherapy.

Study Contact:
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Cancer and Leukemia Group B

Source: NCI Physician Data Query, October 2002

PHASE III RANDOMIZED STUDY OF SURGERY WITH OR WITHOUT AXILLARY NODE CLEARANCE FOLLOWED BY ADJUVANT TAMOXIFEN IN ELDERLY WOMEN WITH BREAST CANCER

Open Protocol

Protocol IDs: EU-93013, IBCSG-10-93, NCI-F93-0008
Projected Accrual: 1,020 patients

Eligibility	Age 60 and older, postmenopausal, stage 1or IIA operable breast cancer, no prior axillary clearance or biopsy allowed
ARM 1	Mastectomy, lumpectomy or quadrantectomy with axillary clearance. Sentinel node biopsy, optional
ARM 2	Patients undergo surgery as in Arm 1 without axillary clearance

All patients receive tamoxifen x 5 years.
Patients in both arms who undergo breast-conserving surgery may receive optional radiotherapy for 5-6 weeks to the remaining breast tissue, chest and lung. Upon recurrence in the conserved breast, patients undergo total mastectomy; those in Arm 2 who experience ipsilateral axillary recurrence undergo surgical excision. Adjuvant tamoxifen and follow-up are continued.

Study Contact:
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International Breast Cancer Study Group

Source: NCI Physician Data Query, October 2002

PROPORTION OF ELDERLY PATIENTS (AGE ≥ 65) IN SWOG TRIALS AS COMPARED WITH THE PROPORTION OF ELDERLY PATIENTS WITH CANCER*

Type of Cancer	% U.S. Cancer Cases Occurring in Patients, ≥ Age 65	% of Enrolled Patients ≥ Age 65
Breast	49%	9%
Brain	44%	19%
Colorectal	72%	40%
Leukemia	63%	27%
Lung	66%	39%
Myeloma	70%	25%
All Types	63%	25%

***The differences between the two groups were significant (P<0.001) for all types of cancer listed.**

Source: 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.

RATES OF OFFERING AND ACCEPTING CLINICAL TRIAL PARTICIPATION IN WOMEN BY AGE

Mean Age (Years)	Offered Protocol	Consented When Offered
50.4	51%	56%
76.5	35%	50%

Kemeny M et al. **Barriers to participation of older women with breast cancer in clinical trials.** *Proc ASCO* 2000;Abstract 2371.

UNDER-REPRESENTATION OF ELDERLY WOMEN IN RECENT CALGB ADJUVANT TRIALS

Trial # Regimens	Total Accrued	Age 70 and older
CLB-8541 CAF in three diferent doses	1572	150 (10%)
CLB-9344 AC ± T	3170	182 (6%)
CLB-9741 A→T→C vs AC→T in a q2 vs q3 wk schedule	2005	162 (8%)

C=cyclophosphamide; A=doxorubicin; F=fluorouracil; T=paclitaxel
Source: CALGB-49907 Protocol.

SELECT PUBLICATIONS

Balducci L. **The geriatric cancer patient: Equal benefit from equal treatment.** *Cancer Control* 2001;8(2Suppl):1-25.

Crivellari D et al. **Burdens and benefits of adjuvant cyclophosphamide, methotrexate, and fluorouracil and tamoxifen for elderly patients with breast cancer: The International Breast Cancer Study Group Trial VII.** *J Clin Oncol* 2000;18:1412-1422.

Du X, Goodwin JS. **Patterns of use of chemotherapy for breast cancer in older women: Findings from Medicare claims data.** *J Clin Oncol* 2001;19:1455-1461.

Extermann M et al. **What threshold for adjuvant therapy in older breast cancer patients?** *J Clin Oncol* 2000;18(8):1709-1717.

Gajdos C et al. **The consequence of undertreating breast cancer in the elderly.** *J Am Coll Surg* 2001;192:698-707.

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Muss HB. **Factors used to select adjuvant therapy of breast cancer in the United States: An overview of age, race and socioeconomic status.** *J Natl Cancer Inst Monogr* 2001;30:52-55.

Zimmick GG, Muss HB. **Systemic therapy for older women with breast cancer.** *Oncology (Huntingt)* 2001;15:280-291; discussion 291-292, 295-296, 299.

LACK OF ELDERLY WOMEN IN CLINICAL TRIALS

Elderly women are typically not enrolled in clinical trials. In the SWOG study of elderly women, published in the New England Journal of Medicine in 1999, Laura Hutchins showed that although "elderly" women comprise 49% of the breast cancer cases in the United States, women over age 65 comprised only 9% of the participants in the SWOG breast cancer trials. We need to increase awareness that women older than 65 can tolerate therapy as well as women younger than 65, that they can derive benefit from treatment as long as their end-organ function is good, and that they should not be excluded from the major clinical trials.

—Edith Perez, MD

EFFECT OF AGE BIAS IN OFFERING CLINICAL TRIAL PARTICIPATION TO OLDER PATIENTS

A lot of physicians in practice, including medical oncologists, have age biases. Many of our trials in the past had age cutoffs. Now 70-year-old women play tennis. We did a study in the CALGB and found that older women were offered trials much less frequently than younger women, but when older woman were offered participation they went on with the same frequency. The data support that older women who are in relatively good health tolerate treatments like chemotherapy, surgery and radiation therapy as well as their younger counterparts. So, physicians need education to overcome these biases.

—Hyman Muss, MD

REASONS FOR LACK OF ELDERLY PATIENTS ENROLLED IN CANCER TRIALS

"Why are the rates of enrollment of elderly patients in trials of treatment for cancer disproportionately low? The reasons include misconceptions about the benefits of enrollment in clinical trials for older patients on the part of the patients themselves, their family members, or their physicians; stringent eligibility criteria; coexisting medical conditions; and logistic barriers.

Clinicians and patients and their families may assume that older patients with cancer are not likely to tolerate or benefit from treatment in clinical trials. They may consider these studies too "experimental" or the treatments too toxic or otherwise inappropriate for older patients. In a survey of American oncologists, 80 percent of the respondents agreed with published data showing that patients have better outcomes when they receive treatment in clinical trials, but 50 percent indicated that they declare patients unsuitable for clinical trials on the basis of age alone…

By 2030, the number of persons in the United States over the age of 65 years will have doubled, and the number of persons over the age of 85 years will have quadrupled. Because of the relatively high risk of cancer in these populations, we predict a high prevalence of cases of cancer in older members of the U.S. population in the future. It may not be premature to implement prospective trials in order to determine why the rates of enrollment of elderly patients in cancer trials are low, to study and modulate the biologic features of cancer in older patients, and to design therapy for otherwise fit older patients with cancer."

—Hutchins LF et al. N Engl J Med 1999;341:2061-2067.