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News

7th World Conference on Lung Cancer

Sponsored by the International Association for the Study of Lung Cancer and the University of Colorado Cancer Center, this conference will be held on 26 June to 1 July 1994 at the Broadmoor Hotel, Colorado Springs, Colorado, U.S.A. This will be the first time since 1978 that this international forum has been held in the U.S.A. The scientific symposia will address the political, scientific and social issues, and controversies relevant to lung cancer through presentations of original research, mini symposia, plenary sessions and poster sessions. Specialists are invited to submit abstracts or original research in the areas of biology, chemotherapy, chemotherapy and surgery, pathology, prevention, pulmonary/imaging, radiotherapy, support and surgery for consideration. To receive further information write to or fax the 7th World Conference on Lung Cancer, Centennial Conferences, 5353 Manhattan Circle, Suite 103, Boulder, Colorado, 80303, U.S.A. Fax 303/499-2599. Tel. 303/499-2299.

20th International Congress on Breast Cancer Research

Under the auspices of the International Association for Breast Cancer Research, the 20th International Congress on Breast Cancer Research will take place on 25–28 September 1994, in Sendai, Japan, organised by Tohoku University School of Medicine. Emphasis will be placed on clinical/research interactions in plenary sessions covering breast cancer genetics, advanced therapies, minimal lesions and intraductal carcinomas, epidemiology, hormone prevention and therapeutic clinical trials, oncogenes and cellular interactions. Workshops covering cell and molecular biology, experimental hormonal studies, genetics, experimental therapeutics, epidemiology and other pertinent topics will also give an opportunity for ample discussion. Poster viewing sessions will present research results of the attendees. Deadline for submission of poster abstracts is 1 April 1994. For information contact Dr R. L. Ceriani, IABCR Secretary General, Cancer Research Fund of Contra Costa, 2055 N. Broadway, Walnut Creek, California 94596, U.S.A. Tel. (510) 943-1167. Fax (510) 943-1189.

Letters

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Long-term Results of a Randomised Trial Comparing Regimens of Cyclophosphamide and Fluorouracil with Either Mitoxantrone or Doxorubicin in Patients With Advanced Breast Cancer

P. Pouillart, J. Y. Follézou, T. Palangie, F. Feuilhade, C. George and E. Richards

LONG-TERM survival is an important criteria in the assessment of the effectiveness of combination chemotherapy in metastatic breast cancer. In a previous article [1] the response rates and safety were reported of a randomised study of two combination regimens for the treatment of advanced breast cancer: cyclophosphamide, mitoxantrone and fluorouracil (CNF), and cyclophosphamide, doxorubicin and fluorouracil (CAF). We report here the long-term results of this study.

Patients were eligible if they had histologically proven and measurable metastatic breast cancer. Patients required a WHO performance status between 0 and 2 and a life expectancy of ≥ 3 months. Normal cardiac function measured by left ventricular ejection fraction (LVEF) or ultrasound, was required. Previous chemotherapy was not permitted, except non-anthracycline adjuvant chemotherapy terminated at least 1 year before enrolment. Patients who were pregnant, had cerebromeningeal metastases, or received hormonal or radiotherapy within 4 weeks of enrolment were excluded. A white blood count $\geq 2 \times 10^9$/l and platelet count $\geq 100 \times 10^9$/l, with normal kidney and liver function were required.

Patients were randomised to receive 600 mg/m^2 of cyclophosphamide, 750 mg/m^2 of 5-fluorouracil, and either 45 mg/m^2 of doxorubicin or 12 mg/m^2 of mitoxantrone administered intravenously, repeated every 3 weeks. Treatment was delayed or dosage reduced in the event of haematological toxicity.

Assessment of responses were made in accordance with World Health Organisation (WHO) criteria [2]. Duration of survival

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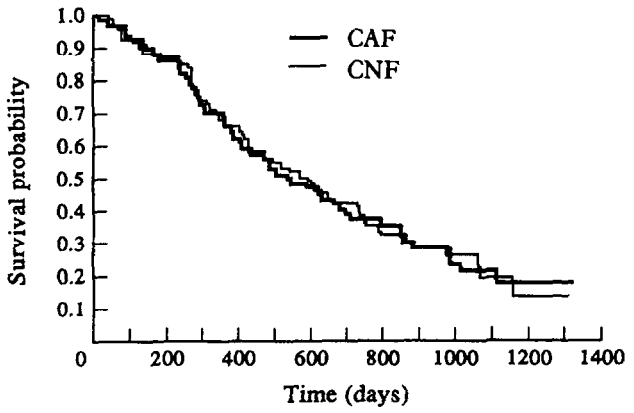

Figure 1. Survival in days as a proportion of all randomised patients surviving from date of entry to date of death.

was defined as the time from randomisation to the last observation or death. Time to disease progression was from randomisation date to the first sign of relapse. Time to event analyses were performed using the Kaplan–Meier method [3,4].

A total of 142 patients were enrolled at 12 sites in France between June 1983 and December 1984. 69 patients were randomised to CNF, and 73 to CAF. As previously reported [1], the two treatment groups showed similar distributions of pretreatment characteristics. For evaluable patients, the overall response (complete + partial response) for CAF was 42% (28/66) with 9 complete responses, and 42% (30/71) for CNF with 6 complete responses, $P > 0.99$ Fisher's exact two-tailed [5].

Both regimens caused myelosuppression, with approximately 45% of patients requiring a reduction and/or delay of therapy dosage. The types, severities and frequencies of the adverse events were similar for both CNF and CAF groups. However, CNF-treated patients had a lower incidence and severity of alopecia, with reports in 51% (222/439) of treatment cycles, 12% (53/439) of these at grade 4, compared to 78% (339/432) for CAF with 44% (189/432) at grade 4 ($P<0.01$). Similarly, nausea and vomiting in the CNF patients were observed in 43% of cycles, with 23% of cycles grade 3 or 4, compared to an incidence of 60%, with 39% grade 3 or 4, in the CAF group ($P< 0.02$). During the treatment phase, moderate and clinically non-significant reduction of left ventricular ejection was observed in 6 of the patients treated with CAF and in 2 of the patients treated with CNF [1].

The survival times for all randomised patients in both treatment groups are shown in Figure 1. There were no statistically significant differences in survival (log rank test, $P = 0.93$). The median survival for CNF was 600 days [95% confidence interval (CI) 426–738] and for CAF 551 days (95% CI 410–743). The estimated hazard ratio was 1.02 (95% CI 0.69–1.49). These survival times are consistent with, or somewhat higher than, previously published reports of these agents in combination therapy in patients with advanced breast cancer [6–8].

For all randomised patients, the median time to disease progression was 233 days (95% CI 147–272) for CNF and 182 days (95% CI 145–294) for CAF, with no statistically significant difference (log rank test $P = 0.43$), and an estimated hazard ratio of 0.86 (95% CI 0.61–1.23).

The long-term follow-up requested reports of severe adverse events and their relationship to protocol therapy. A total of 20 adverse events were reported, 12 on CNF and eight on CAF. Four cardiovascular events were reported during the follow-up phase for patients initially randomised to CAF with two reported on CNF. A case of thrombocytopenia was thought to be possibly related to CNF treatment, and one case of pulmonary oedema to CAF. All other reported severe adverse events were related to therapy administered subsequent to completion of the study.

The survival data from this clinical trial indicates that mitoxantrone is equally as effective as doxorubicin in combination with cyclophosphamide and 5-fluorouracil in the treatment of women with advanced breast cancer.

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Detection of Platinum–DNA Adducts in Cord Blood Lymphocytes Following *In Utero* Platinum Exposure

O.N. Koc, M. McFee, E. Reed and S.L. Gerson

ASSESSING THE impact of chemotherapy on the fetus of patients treated for a malignant disease during pregnancy has been limited to epidemiological analysis of clinical outcomes.

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