of margins; and (3) the optimal sequence and timing for radiation therapy and systemic adjuvant therapy.

The conclusions adopted by the consensus panel are likely to have an important influence on the treatment policy of early breast cancer throughout the world. The acceptance without reservation of the principle of breast conservation by appropriate combined surgical-radiological procedures will influence medical opinion, convincing the profession of the need to proceed in the direction of less mutilating procedures whenever such techniques will obviously not interfere with survival rates, so that breast cancer patients, once cured of their disease, will enjoy a life as close to normal as possible. This will, in turn, increase the confidence of women that they will receive more humane treatment and will stimulate their participation in prevention and detection programmes.

Eur J Cancer, Vol. 26, No. 7, pp. 844–845, 1990.
Printed in Great Britain
02 7-5379/90$3.00 + 0.00

Adjuvant Chemotherapy in Node-Negative Breast Cancer NCI Consensus Conference

Gianni Bonadonna

THE DATA from six randomised clinical trials on adjuvant chemotherapy in node-negative breast cancer were presented at the National Cancer Institute consensus conference. Overall, despite differences in patients' selection criteria, drug combination, dose intensity and duration of adjuvant treatment, it was felt that adjuvant chemotherapy can reduce the rate of disease recurrence by about a third. To date mortality has been reduced in nearly all trials but the decrease has not been statistically significant in most. However, the rate of death in node-negative patients is low, so a clinically important reduction in mortality may require a long follow-up to achieve statistical significance. Among the various chemotherapy regimens, more benefit was seen in trials in which antimetabolites were administered intravenously than in trials in which such drugs were given orally. The results of the six trials can be summarised as follows.

The Swiss investigators [1] reported an increased, albeit not statistically significant, 14 year relapse-free and overall survival favouring patients treated with oral chlorambucil, methotrexate, and fluorouracil (LMF) given for 6 months, followed by BCG immunotherapy up to relapse or 2 years. 122 node-negative patients entered the study, but no attempts were made to select patients with unfavourable prognosis.

The 7-year results of the study performed at the Milan Cancer Institute [2] showed that women with node-negative and oestrogen receptor (ER) negative breast cancers benefitted from intravenous cyclophosphamide, methotrexate and fluorouracil (CMF) administered every 3 weeks for twelve courses. Both relapse-free (control 42% vs. CMF 85%, $P = 0.0001$) and overall survival (58% vs. 86%, $P = 0.006$) were statistically significant and results were not influenced by menopausal status or tumour size. Only 90 patients could be entered into the study. In both treatment groups, half the tumours were histologically classified as highly undifferentiated (grade 3) and two-thirds had high proliferative activity.

In the West Midlands Oncology Association trial [3], 574 unselected patients were randomised to receive either simple mastectomy with axillary sampling or the same plus oral LMF for eight cycles. At the 5-year analysis, no difference in outcome was evident either in terms of relapse-free or overall survival. When the effect of prognostic factors was analysed, regardless of the treatment assigned, patients presenting with poorly differentiated tumours were at a high risk of disease relapse ($P = 0.0006$) and death ($P = 0.0001$) compared with women with moderately or well differentiated tumours.

Investigators of the International Breast Cancer Study Group [4] reported their experience in 1275 unselected patients with node-negative tumours, two-thirds of whom received one cycle of perioperative intravenous CMF. After a median follow-up of 5 years, women who received perioperative CMF had a significantly greater relapse-free survival (74%) than patients in the control arm (68%, $P = 0.03$), but the overall survival was not different between the two groups. The treatment effect was large for patients with ER-negative tumours and the greatest benefit was observed in ER-negative postmenopausal women, both in terms of relapse-free (79% vs. 56%, $P = 0.0003$) and overall survival (91% vs. 70%, $P = 0.0008$).

425 patients with node-negative and either ER-positive tumours measuring 3.0 cm or more or ER-negative tumours of any size were entered into the Intergroup Study [5]. Women were randomised to either observation or to six cycles of CMF plus prednisone (CMFP). The 5 year relapse-free survival was 61% vs. 83%, respectively ($P < 0.0001$). A treatment benefit was observed in premenopausal and postmenopausal women as well as in patients with ER-positive or ER-negative tumours, but patients in the untreated group with ER-positive tumours measuring 3 cm or more had the most unfavourable prognosis—only 42% were free of disease relapse. Overall, 86% of women treated with CMFP were alive at 5 years compared with 80% in the observation group.

The National Surgical Adjuvant Breast and Bowel Group studied patients with node-negative and ER-negative tumours. 737 eligible women were randomised to methotrexate followed by fluorouracil for twelve cycles or to no postoperative therapy. 5 year analysis indicated a significantly prolonged relapse-free survival ($P = 0.0007$) in the treated group. The benefit was unrelated to menopausal status, tumour size, and type of surgery (total mastectomy or lumpectomy) and both local–regional and distant metastases were decreased. A trend towards an improved 5 year overall survival favouring untreated patients ($P = 0.09$) was also observed.

As far as prognostic factors that may influence treatment decision-making are concerned, the consensus panel made the following points: (1) in general, the risk of recurrence increases with increasing tumour size; (2) patients with hormone receptor positive tumours have a better prognosis than those with receptor negative tumours; (3) high nuclear grade is associated with a higher rate of relapse; (4) measurements of cellular proliferation in breast cancer specimens have a strong correlation with outcome; (5) high levels of the protease cathepsin D are associated with unfavourable prognosis; and (6) HER-2/*neu*, epidermal growth factor receptor and stress-response (heat shock) proteins require further investigation.

The many unanswered questions about the adjuvant systemic treatment of node-negative breast cancer make it imperative

Correspondence to G. Bonadonna, Division of Medical Oncology, Istituto Nazionale Tumori, 20133 Milano, Italy.

that all patients who are candidates for clinical trials be offered the opportunity to participate. However, there are extremes of high and low risk where it is possible to make recommendations about adjuvant systemic chemotherapy outside the context of prospective trials.

Among the other statements of the panel, it is worth mentioning that more patients with node-negative breast cancer are cured by optimal local–regional treatment. The decision to use adjuvant chemotherapy should follow a thorough discussion with the patient about the likely risk of relapse after local–regional therapy alone, the expected reduction in risk with postoperative chemotherapy, and treatment-related toxicity and its possible impact on quality of life.

All citations are abstracts published in the proceedings.
1. Jungi WF, Senn HJ. Swiss adjuvant trials in women with node negative breast cancer: 14-year results.
2. Bonadonna G. Milan adjuvant chemotherapy trial for node negative breast cancer patients.
3. Morrison JM, Kelly KA, Howell A, *et al.* The West Midlands Oncology Association trial of adjuvant chemotherapy for patients with node negative breast cancer.
4. Goldhirsch A, Castiglione M, Gelber RD. International Breast Cancer Study Group trial of perioperative chemotherapy.
5. Tormey DC, Eudey L, Mansour EG, *et al.* Int-0011: CMFP versus observation in high-risk node negative breast cancer patients.
6. Fisher B, Redmond C, and Contributing NSABP Investigators. NSABP B-13: methotrexate + 5-FU in women with estrogen receptor negative, node negative breast cancer.

News

Neuro-oncology Conference

The Second International Neuro-oncology Conference, in memory of Professor H.J.G. Bloom, will be held at the Royal Marsden Hospital, London, on 25–26 March 1991. The conference, on tumour-directed therapy of brain tumours, will include sessions on tumour localisation, stereotactic radiotherapy and radiosurgery, stereotactic surgery, interstitial radiotherapy, intralesional and intra-arterial chemotherapy, and immunotherapy. For further information please contact Dr Michael Brada, Royal Marsden Hospital, Downs Road, Sutton, Surrey, SM2 5PT, U.K. Tel (44) 81 642 6011 ext 3272/4, fax (44) 81 643 1725.

Urological Oncology Symposium

The Third International Symposium on Advances in Urological Oncology will be held on 7–9 March 1991 in Sanremo, Italy. The symposium will discuss problems relating to the management of testicular tumours. Further information can be obtained from Dr F. Boccardo, Department of Clinical Oncology, National Institute for Cancer Research, Vle Benedetto XV, 10-16132 Genoa, Italy. Tel (39) 10 352753.

Steroid Biochemistry and Molecular Biology

The 10th International Symposium of the Journal of Steroid Biochemistry and Molecular Biology, 'Recent Advances in Steroid Biochemistry and Molecular Biology', will be held in Paris, France from 26–29 May 1991. The symposium will consider the following topics: steroid receptor structure, gene expression and molecular mechanisms; steroid hormones, anti-steroids, growth factors, oncogenes, and cancer; steroid hormones in reproduction; enzymatic control of steroid production; and steroids and hypertension. In addition to invited lectures there will be a poster session and abstracts should be submitted to Dr J.R. Pasqualini, CNRS Steroid Hormone Research Unit, Foundation for Hormone Research, 26 Boulevard Brune, 75014 Paris, France. Tel (33) 1 45 39 91 09, fax (33) 1 45 42 61 21.

Breast Cancer Conference

The 5th Breast Cancer Working Conference, organised by the EORTC Breast Cancer Cooperative Group, will be held in Leuven, Belgium, on 3–6 September 1991. The conference will include teaching lectures, technical workshops, symposia, and proffered paper and poster sessions, with emphasis on innovative approaches in basic research as well as on different diagnostic techniques in breast cancer. For further information contact the Conference Secretariat EORTC-BCWC, University Hospital St Rafael, Department of Radiotherapy, Kapucijnenvoer 33, 3000 Leuven, Belgium.

Myelodysplastic Syndromes

An international workshop on 'Therapy of Myelodysplastic Syndromes: Advances and Perspectives' will be held in Innsbruck, Austria, on 7–10 October 1990. For further information please contact Dr H. Zwierzina, Universitatsklinik fur Innere Medizin, Anichstrasse 35, A-6020 Innsbruck, Austria.

Cytokine Consensus

A consensus meeting of the 'Cytokine Task Force', part of the EORTC Research Branch, will be held in Esseu on 23–24 November 1990. For further details please contact the organiser: Dr H. Zwierzina, Universitatsklinik fur Innere Medizin, Anichstrasse 35, A-6020 Innsbruck, Austria.

Immunodeficient Mice in Oncology

The international symposium on the 'Use of Immunodeficient Mice in Oncology' will be held in Freiburg, F.R.G., on 7–9 November 1990. Further information can be obtained from Dr D.P. Berger, Department of Internal Medicine I, Haematology/Oncology, University of Freiburg, Hugstetterstr. 55, D-7800 Freiburg, F.R.G.

U.C. San Diego Cancer Center Conferences

The University of California San Diego Cancer Center are planning a series of three conferences to be held in California between October 1990 and March 1991.

The Society for Complex Carbohydrates 19th Annual Meeting 'Glycobiology in San Diego' will be held at La Jolla, California, U.S.A. on 10–13 October 1990.

The 6th International Symposium on Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy will be held in San Diego, California, U.S.A. on 23–26 January 1991.

The Sixth International Conference on Monoclonal Antibody Immunoconjugates for Cancer will be held in San Diego 28 February–2 March 1991.

Further information on these meetings can be obtained from Cass Jones, Professional Conference Management Inc., 7916 Convoy Court, San Diego, California 92111, U.S.A. Tel (1) 619 565 9921.