S35 CEF versus CMF in premenopausal women – Recent update

M. Levine, V. Bramwell, K. Pritchard, L. Shepherd. *National Cancer Institute of Canada Clinical Trials Group, Canada*

The results of clinical trials evaluating the efficacy of anthracycline chemotherapy in axillary node positive breast cancer have been inconclusive. Premenopausal women with node positive breast cancer were randomly allocated to receive either cyclophosphamide (100 mg/m^2 orally, Days 1–14), methotrexate (40 mg/m^2 IV, Days 1 & 8) and fluorouracil (600 mg/m^2 IV, Days 1 & 8) (CMF) or cyclophosphamide (75 mg/m^2 orally, Days 1–14), epirubicin (60 mg/m^2 IV, Days 1 & 8) and fluorouracil (500 mg/m^2 IV, Days 1 & 8) (CEF). Each cycle was administered monthly for six months. Patients on CEF received antibiotic prophylaxis with cotrimoxazole two tablets twice a day. The median follow-up is 59 months. 169 (47.1%) of the 359 CMF patients developed recurrence compared to 132 (37.6%) of the 351 CEF patients. The corresponding 5 year relapse-free survivals are 53% and 63% respectively, P = 0.009. 107 (29.8%) CMF patients have died compared to 85 (24.2%) CEF patients; 5 year survivals are 70% and 77% respectively, P = 0.03. There was one case of congestive heart failure in a patient who received CMF compared to none in the CEF group. Acute leukemia occurred in five patients in the CEF group. The results of this trial demonstrate the superiority of CEF over CMF in terms of both relapse-free survival and overall survival in premenopausal women with axillary node positive breast cancer.

S36 New developments in high-dose chemotherapy for breast cancer

Russel Basser. *Department of Clinical Haematology and Medical Oncology, Royal Melbourne Hospital and Western Hospital, Vic, Australia*

Breast cancer is now the most common indication for high-dose chemotherapy (HDC) with autologous stem cell support in the USA. This activity is based on promising results from numerous phase 2 studies, although there are now data from at least 3 small randomized trials. Most approaches employ standard-dose induction therapy followed by a single myeloablative dose. However, a number of investigators have reported results of high doses of single agents with cytokine and stem cell support (high-dose sequential therapy), or multiple cycles of non-ablative therapy with stem cell support. While the patients initially treated with HDC had metastatic breast cancer, a shift in focus has occurred so that many studies are now investigating the efficacy of HDC in patients with poor prognosis, early stage disease. We developed a regimen of 3 cycles of dose-intensive epirubicin 200 mg/m^2 and cyclophosphamide 4 mg/m^2 with stem cell given after each cycle in a pilot study of 100 patients with 10+ nodes. The median follow-up of surviving patients is now 40 months, and long-term morbidity is low. The efficacy of this treatment is now being tested in a randomized trial (IBCSG 15). Cautionary evidence of the selective nature of pilot studies of HDC in breast cancer has recently emerged that supports the need for completion of randomized studies prior to widespread adoption of this approach as a standard of care.

An important issue of uncertain significance is that of tumor cell contamination of blood products. A large number of studies have documented the presence of circulating breast cancer cells using sensitive immunohistochemical techniques or reverse transcriptase PCR. The presence of such cells is almost certainly predictive of early relapse of disease. While methods have been established to reduce the load of tumor cells infused into patients in stem cell collections after HDC without adversely affecting hematopoietic recovery, there is no proof that this improves patient outcome. Furthermore, assays for detection of circulating tumor cells have not been standardized, so that interpretation of the reported frequency of contamination of bone marrow and apheresis products (anywhere from 12% to 67%) is difficult.

Emerging technologies hold exciting prospects for further improving breast cancer treatment. Monoclonal antibodies to cellular oncogenes, such as her2/neu, have already been demonstrated to possess clinical activity, and are currently being evaluated in conjunction with standard-dose chemotherapy. Oncostatin M has recently been shown to inhibit hormone receptor-negative breast cancer cell growth *in vitro*, and is currently being assessed in preclinical *in vivo* models. Finally, agents that prevent the growth of cancer through inhibition of angiogenesis or tumor stroma raise the hope of treatments that circumvent the problems associated with chemotherapy resistance.

Friday, February 27, 1998 **17.00–18.00**

Session 10 Integrated Treatments: Quality of Life

S37 Quality of life assessment in the adjuvant setting: Is it relevant?

R.D. Gelber, S. Gelber, M. Bonetti, A. Goldhirsch. *Dana-Farber Cancer Institute and Frontier Science and Technology Research Foundation, Boston, MA, USA; European Institute for Oncology, Milan, for the International Breast Cancer Study Group (IBCSG), Italy*

In the adjuvant setting, the critical issue to consider in treatment decision-making is the trade-off between quality and quantity of life. The toxicities of adjuvant therapies must be balanced against the potential benefits of delayed recurrence and improved survival. In this presentation, we consider when quality-of-life assessment is relevant in this setting. Such assessments can inform patients about what to expect from their treatment, describe quality-of-life differences between treatments, provide an additional baseline measure with potential prognostic significance, inform clinicians about their patients' experiences with toxicities, indicate situations in which psychosocial interventions might be useful, and document patient adaptation to diagnosis and treatment. The relevance of quality-of-life assessment in the adjuvant setting will be illustrated by investigating one of the most controversial questions of today: when should chemotherapy be added to tamoxifen for postmenopausal patients? Data from the IBCSG Trial VII (J Clin Oncol 15:1385–1394, 1997) showed that adding three months of CMF (cyclophosphamide 100 mg/msq orally days 1–14; methotrexate 40 mg/msq i.v. days 1, 8; fluorouracil 600 mg/msq i.v. days 1, 8; repeated every 28 days) to Tamoxifen significantly improved disease-free survival compared with Tamoxifen alone. The Quality-adjusted Time Without Symptoms of disease or Toxicity of treatment (Q-TWiST) method was used to compare the adjuvant therapies with respect to quality-adjusted survival. The analysis indicated that the decision to use adjuvant chemotherapy in this setting should be based on patient preferences concerning the relative importance of treatment toxicity versus disease recurrence.

S38 Quality of life measurements in the IBCSG: Past, present and future

Ch. Hürny, J. Bernhard, A. Coates. *International Breast Cancer Study Group (IBCSG), Switzerland*

Past: Since 1986, the IBCSG is accruing a comprehensive longitudinal health-related Quality of Life (QL) data base in addition to biomedical data of patients with early breast cancer under and beyond adjuvant treatment with the aim to establish QL as a complementary outcome in randomized clinical trials and to get new insight in biopsychosocial interactions. Concerning methodology the IBCSG has made major contributions to the field in the development of global indicators, cross-cultural validation, impact of timing of assessments and working on practical and statistical issues of missing data.

Present: In two large-scale clinical trials (IBCSG VI and VII) adjuvant chemotherapy had a measurable adverse effect on health-related QL, but contrary to expectations this effect was transient and minor compared with patients adaptation/coping after diagnosis and surgery.

Future: In addition to the assessment of health-related QL the IBCSG is currently developing and applying a global indicator for a patient derived adapted utility concept in order to better assess the cost-benefit ratio of adjuvant treatment. However, the real challenge for the immediate future is the question how patients adaptation can be fostered within primary care.

S39 Impact of different adjuvant therapy strategies on quality of life (QOL) in breast cancer survivors (BCS)

P.A. Ganz[1], J. Rowland[2], B.E. Meyerowitz[3], K. Desmond[1]. [1]*UCLA, Los Angeles, CA, USA;* [2]*Georgetown University, Washington, DC, USA;* [3]*USC, Los Angeles, CA, USA*

Little is known about the long-term effects of adjuvant therapy on QOL and sexual functioning in BCS. Between January 1996 and June 1997, we surveyed 1,110 BCS who had been diagnosed with early stage breast cancer between 1 and 5 yrs earlier (average 2.8 yrs since diagnosis). The BCS were recruited in two large metropolitan cities in the U.S.A. BCS completed a survey battery that contained standardized measures of QOL (MOS-SF-36, Ladder of Life), mental health (MOS Mental Health Index, CES-D), symptoms, social support, body image, marital/partner functioning, and sexual functioning. In this sample,