Thursday, 1 October 1998 **16:00-18:00**

PARALLEL SESSION

Systemic therapy: focus on the adjuvant setting

160 INVITED

New challenges in the medical treatment of breast cancer

L. Gianni. *Division of Medical Oncology, Istituto Nazionale Tumori, Milano, Italy*

The use drugs plays a pivotal role together with local-regional modalities at all stages of breast cancer. In addition, cytotoxic and hormonal drugs are no longer perceived as alternative options. In the past 20 years, the success of medical treatment has been substantial, but management of women with breast cancer is still not curative in many patients. This consideration comes at a time when completely new classes of drugs are becoming available, such as anti-angiogenic, anti-metastatic compounds, and specific inhibitors of different signal-transduction pathways. These new drugs represent a long-waited opportunity, and challenge investigators in the field to innovative development and inclusion of these new drugs in the standard approach. One important goal of new treatment strategies will be that of defining criteria for specific indication of drugs so that therapy will no longer benefit the "average" patient defined within a broad category of risk, but will be tailored to individual characteristics predicting for response. The rational design of the new compounds offers an unprecedented opportunity to explore such an individualised use of new drugs alone or in combination with cytotoxic or hormonal compounds.

161 ORAL

Long term survival of patients treated with neoadjuvant chemotherapy for operable breast tumors: Results of a randomized trial with a 10 year-follow-up

L. Mauriac, G. Mac Grogan, M. Durand, A. Avril, J.M. Dilhuydy. *For the IBBGS (Institut Bergonié Bordeaux Groupe Sein), France*

In 1991, we published a randomized trial comparing first line mastectomy to neoadjuvant chemotherapy for patients with too big breast tumors to be operated on by initial breast conserving surgery (Ann Oncol 1991; 2: 347–54). Patients treated with modified radical mastectomy received afterwards an adjuvant chemotherapy if they had either an axillary nodal involvement or an absence of estrogen and progesterone receptor. In the other treatment arm, neoadjuvant chemotherapy was the same as adjuvant and was followed by an adjusted locoregional treatment according to residual tumor: exclusive irradiation, conservative surgery with breast irradiation or modified radical mastectomy without irradiation. Conserving treatment rates were of 63% after neo-adjuvant chemotherapy, more frequent in case of absence of steroid receptor (EPR$^-$) (73%). At 124-month median follow-up, 45% of patients still have their breast conserved while this rate is higher for patients with EPR$^-$ tumors (55%). With a 124-month median follow-up (min. 97, max. 148 months) actuarial overall survival is identical in the 2 treatment arms. Furthermore, there is no difference in terms of metastatic and local recurrence-free survival. An unifactorial analysis of prognostic factor of overall survival shows that progesterone receptor negativity, c-erbB2 positivity and Mib1 > 40% (antiKi-67), analysed by immunohisto-chemistry are predictive of poor survival in the group of patients treated by neoadjuvant chemotherapy. But multivariate analysis shows that only c-erbB2 > 0 is an independent prognostic factor for overall survival and metastatic-free survival.

162 ORAL

Randomised trial of long-term adjuvant tamoxifen plus postoperative radiation therapy versus radiation therapy alone in patients with early-stage breast cancer treated with breast-conserving surgery

Kristina Dalberg[1], Hemming Johansson, Ulla Johansson, Lars E. Rutqvist. [1]*Department of Surgery, Oncologic Centre, Karolinska Hospital, Stockholm, Sweden*

Introduction: The use of adjuvant tamoxifen in postmenopausal breast cancer patients as an adjunct to primary surgery is well established. The present study reports long-term results from a low-risk stratum in a randomised trial of adjuvant tamoxifen. The main focus of this analysis was if node-negative postmenopausal patients treated with breast-conserving surgery and postoperative radiotherapy would benefit from tamoxifen in terms of a reduced local failure rate.

Patients and Methods: The study population included 432 node-negative postmenopausal patients with invasive breast cancer (T1-T2) who underwent breast-conserving surgery followed by radiotherapy in Stockholm 1976–1990. The patients constituted a separate stratum of the Stockholm Adjuvant Tamoxifen Trial which included a total of 2729 patients. 213/432 patients received 40 mg tamoxifen daily for 2 or 5 years. The median follow-up time was 8 (5–19) years.

Results: The event-free survival at 10 years was 80% in the tamoxifen group and 70% in the control group (p = 0.03). Tamoxifen reduced the overall rate of ipsilateral (relative hazard (RH) = 0.4; 95% confidence interval (CI) = 0.2–0.9, p = 0.02) and contralateral breast tumor recurrences (RH = 0.4; CI = 0.1–1.1, p = 0.06). Trends towards a reduced number of distant metastases (RH = 0.6; CI = 0.3–1.2, p = 0.1) and deaths due to breast cancer (RH = 0.5; CI = 0.2–1.2, p = 0.1) were also observed.

Conclusion: The addition of tamoxifen to radiotherapy in postmenopausal, node-negative breast cancer patients treated with breast conserving surgery is advisable, since a reduced rate of ipsilateral and contralateral breast tumor recurrences may be accomplished. The results raise the issue of whether tamoxifen might replace radiotherapy in women with estrogen receptor-positive, node-negative breast cancer disease at low risk for local relapse.

163 ORAL

Adjuvant CMF +/− tamoxifen (TAM) in premenopausal high-risk patients (PHRPs) with early breast cancer

M. Andersson[1], C. Kamby[2], C. Rose[3], J. Andersen[4], M.-B. Jensen[5], H.T. Mouridsen[1,5]. *On behalf of the Danish Breast Cancer Co-operative Group (DBCG); Dpt. Oncology University Hospitals of [1]Copenhagen; [2]Herlev; [3]Odense; [4]Aarhus; [5]DBCG Secretariat, Copenhagen, Denmark*

Purpose: In PHRPs to evaluate whether combined CMF + TAM is superior to CMF alone with regard to recurrence free survival (RFS) and overall survival (OS).

Methods: Following modified radical mastectomy 314 PHRPs (node+ and/or tumor >5 cm) were randomised to receive CMF alone (Cyclophosphamide 600, Methotrexate 40, Fluorouracil 600 mg/m^2 iv. q 4 weeks, 9 cycles) and 320 to receive CMF + TAM 30 mg daily for one year.

Results: Patients were well balanced with regard to the prognostic factors: tumour size, age, no. of positive nodes, ratio of positive to total no. of nodes removed, degree of anaplasia and receptor status (CMF + TAM vs CMF: receptor positive: 38% vs 41%, negative: 12% vs 12%, unknown: 50% vs 47%). Ten-year RFS were 34% vs 35% (p = 0.81) and 10-year OS 45% vs 47% (0.73). In a Cox proportional hazards model no significant interactions between treatment and prognostic factors including receptor status were found.

Conclusion: In PHRPs with mixed receptor status given adjuvant chemotherapy, the addition of one year treatment with Tamoxifen does not improve RFS or OS.