diagnosed BCs in the region). At first visit a checklist with 8 presumed risk factors is used. To patients who have one or more risk factors the composition of an extensive family tree is proposed. Information concerning the family history of BC (age at diagnosis, bilaterality) and the occurrence of other cancers such as ovarian cancer is taken into account. Guided by specific criteria, referral to the Family Cancer Clinic at the UH is suggested. GC and DNA testing for BRCA1 and BRCA2 mutations is offered to selected patients. In this study insight will be gained in the interest of unselected BC patients and their families for GC and DNA testing. In addition the correlation between several risk factors, the probability of hereditary BC and the detectability of DNA mutations is studied. During the first 8 months 304 patients were registered. 132 patients had 1 or more risk factors: 85 of them agreed with the construction of a family tree, 51 fulfilled the criteria for referral to the Family Cancer Clinic and 35 accepted GC. Preliminary results will be presented.

549 POSTER

CIP-1 Protein expression in node-positive breast cancer patients

P. Hupperets[1], E. Thunnissen[2], J. Peterse[3], H. Schouten[1]. *Departments of [1]Internal Medicine; [2]Pathology, University Hospital Maastricht; [3]Department of Pathology, Netherlands Cancer Institute, Amsterdam, The Netherlands*

CIP-1 is a cyclin dependent kinase inhibitor which negatively controls cell proliferation. Since chemotherapy may affect cell cycle regulation, in this study the hypothesis was tested that increased levels of CIP-1 may be associated with poor response to chemotherapy and with dismal clinical outcome. CIP-1 protein was assessed by immunohistochemistry (IHC) in 26 node-positive breast cancer patients (pts) (≥10 tumor containing axillary nodes or tumor containing infraclavicular node). All 26 pts had been treated with 4 cycles of conventional chemotherapy followed by high-dose chemotherapy supported by bone marrow stem cells. In 1 pt no tumor was left in the paraffin section for IHC. Nuclear staining for CIP-1 was observed in tumor cells in 18/25 of tumors (with usually moderate (+) and sometimes equal intensity (++) compared to internal controls). Nine of the pts with this staining had no evidence of disease (NED) after a median follow-up of 3 yrs, whereas 8 had recurrent disease. Five pts without this staining pattern (intensity 0 or ±) had NED, whereas 2 pts died, one with, and one without disease. Nuclear staining for CIP-1 in an estimated area of >50% of tumor area was observed in 18/25 of tumors. No differences in clinical outcome could be detected: 10 pts with nuclear staining of >50% of tumor area had NED, whereas 8 pts had recurrent disease. Those pts with minimal or absent nuclear staining (≤10% of tumor area) (3 pts) had NED. CIP-1 expression is found in a high percentage of nuclei in breast cancer tumor cells of pts with bad prognosis breast cancer. CIP-1 expression is not associated with clinical outcome in these heavily treated pts, whereas the absence of CIP-1 expression seems to be associated with good prognosis.

550 POSTER

A study of correlation between DNA ploidy pattern and aberration of chromosome 8 detected by fluorescence in situ hybridization in human breast cancer

S. Hara, R.S. Terada, H. Ayabe, Y. Tagawa. *Nagasaki University School of Medicine, First Department of Surgery, 1-7-1 Sakamoto, Nagasaki-city, J-8528501 Nagasaki, Japan*

Purpose: To compare DNA ploidy pattern (DP) by flow cytometry (FCM) with the aberration of chromosome 8 (Chr.8) by fluorescence in situ hybridization (FISH) in human breast cancer and to study the correlation between them with axillary lymphnodes metastasis.

Methods: Fifty cases of breast cancer which had no chemotherapy and radiation therapy before radical operation were studied. Tissues obtained by operation were divided two sections. The one were sliced and DP were analyzed by propidium iodide staning using FCM (FACScan). The stump sections were made from the others and fixed with acetone, and aberration of Chr.8 were analyzed on 200 cancer cells by FISH using D8Z1/biotin (Oncor) probe which detects centromere of chr.8.

Results: Thirty-three (66%) of 50 had DNA aneuploidy, 17 (34%) had DNA diploidy. The aberration rates of Chr.8 widely ranged from 19 to 75%. There was no significant correlation between DP and aberration rates of chr.8. There was significant correlation only between axillary lymphnodes status and aberration rates of chr.8 ($p = 0.023$). There was no correlation between DP and axillary lymphnodes status.

Conclusion: These results show that breast cancer with high aberration rates of chr.8 tend to involve axillary lymphnodes.

551 POSTER

The antioxidant status of breast cancer patients

D. Korman. *Laboratory of Oncology, Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Russia*

The different changes of AOS have been established at various pathological processes including cancerogenesis and tumor growth. The extent of unsaturation of the tissues and blood lipids, which can be defined by the number of double bounds (C = C) in lipids (NDB), may be considered as an integral parameter for the AOS of a tissue and whole body characterization.

We determined NDB in lipids extracted from blood plasma and erytrocytes before treatment in 113 breast cancer patients (BCP) and 94 healthy women. NDB was measured using the special device -"double bounds analysator – DBA". It was discovered that NDB was significantly higher in the lipids of BCP than in that of controls and correlated with the extent of tumor. The patients with advanced (stage IV) BC had mean value of NDB $3.5 \div 0.3 \times 10^{18}$/mg of lipids, with operable BC – $1.8 \div 0.3 \times 10^{18}$, with benign breast tumors – $0.2 \div 0.05 \times 10^{18}$, in control – $0.4 \div 0.03 \times 10^{18}$. The higher DB level was corresponded to various unfavorable prognostic clinico-morfological factors.

The changes of NDB in blood lipids are considered as a reflection of the tumor-host interrelations. The assay of this parameter in cancer patients may be useful for define tumor extent, for monitoring of patients status and results of treatment, for determination of indications for treatment with antioxidants.

552 POSTER

Presurgery chemotherapy and DNA ploidy of the adenocarcinoma breast cells

T. Nikolaeva, Ya. Dobrynin. *N. Blokhin Cancer Research Center RAMS, Moscow 115478, Russia*

Purpose: To evaluate effectiveness of adenocarcinoma breast (AB) preoperation chemotherapy (PC).

Methods: We studied by FCM the changes of DNA synthesizing cells fraction (SF) (19 cases) and ploidy (29 cases). The biopsies was taken before and after course of PC during surgical operation.

Results: Discovered reduce SF cells after clinically successful treatment in 13 pts with diploid AB. The mean life time this pts was 4 years, 4 pts survived 6 years. In 6 nonresponders to treatment showed the increase the SF cells in all cases. In this group the recurrence onset was detected at 8–18 mo. and the mean life time was less than 2 years. FCM analysis before PC treatment demonstrated in 17 cases DNA content like diploid (D) and in 12 ones aneuploid (A). The analysis after PC showed the diploidy in 12 cases (1 group) and aneuploidy in 8 ones (IY group). 5 D tumors became A ones (II group), 4 A tumors became D ones (III group). 2 pts (16.7%) of the I group have recurrences through 25 and 11 mo. and died through 36 and 20 mo., 10 pts lived 57–80 mo. 3 (65%) pts of the II group have recurrences after 10–12 mo. and died shortly (12–15 mo.), 2 (33%) pts with D tumors becoming tetraploid after PC. They have not recurrences and lived 52–86 mo. In 2 cases (III group) the modification of A population (hyperdiploid) into D led to rapid progression of the disease (10–12 mo.) and pts died through 15–50 mo. The modification A population in any site (IY group, 7 cases) accompanied the disease progression and reduced survival length (6 pts died through 24–49 mo.).

Conclusion: The conservation D or tetraploidy after PC is prognostic factor of the PC efficacy in AB pts in III stage of the decease.

553 POSTER

p-Glycoprotein (pGP) and p53 expression in primary breast cancer

P.G. Betta[1], G. Bottero[1], M.F. Cosimi[1], G. Spinoglio[1], M. Pavesi[2], M. Pastormerlo[2]. *[1]Department of Oncology, Azienda Ospedaliera, Alessandria; [2]Unit of Pathology, Santo Spirito Hospital, Casale Monferrato, Italy*

Purpose: To assess the putative relationship between the expression of multidrug resistance-associated protein (pGP) and p53 protein accumulation in primary breast cancer surgical specimens (n = 40).

Methods: Immunohistochemistry with monoclonal antibodies JSB1 (anti-pGP) and DO7 (anti-p53) using a streptavidin/biotin/HRP technique on paraffin sections.

Results: pGP staining was strong in 10 (25%) and weak in 18 (45%) specimens. Among the 28 pGP +ve cases, DO7 labelling was found in 12 (43%), whereas in the remaining 12 pGP −ve cases 4 were p53 +ve.

Conclusion: No significant relationship (χ^2-test: >0.05) was observed between pGP and p53 expression and therefore p53 accumulation does not stimulate pGP expression in primary breast cancer.

(This work was financially supported by the Italian League against Cancer, section of Alessandria).

554 POSTER

Induction of PCD with doxorubicin in invasive lobular carcinoma cells of human breast by circumventing MDR-1 with colloidal phosphorothioate

J. Giannios, P. Ginopoulos. *Dept of Internal Med., Onc. Div., Med. School, University of Patras, Greece*

Antisense oligonucleotides such as phosphorothioate was entrapped in DRV colloidal particles for circumvention of intrinsic resistance to chemotherapy. Invasive lobular carcinoma cells of human breast exhibited enhanced expression of MDR-1 immunocytochemically. Pgp synthesis was inhibited after incubation of these tumor cells with colloidal phosphorothioate for 8 hours at 37°C. Combined administration of doxorubicin has induced D2 stage of apoptosis and bystander effect after 72 hours post-incubation, according to electron microscopy analysis. Thus, colloidal phosphorothioate has reversed MDR allowing doxorubicin influx which leads to PCD and subsequent bystander effect, eradicating the chemoresistant lobular carcinoma.

Friday, 2 October 1998 16:00-18:00

PARALLEL SESSION

Psychosocial oncology

559 INVITED

Psychosocial oncology: Where are we now?

Ann Cull. *ICRF Medical Oncology Unit, Western General Hospital, Edinburgh EH4 2XU, UK*

The origins of psychosocial oncology derive from concerns about the psychological consequences of mutilating surgery in the treatment of breast cancer. Psychosocial oncology has now come of age as discipline. As this symposium will demonstrate it is now addressing a wide range of issues across the spectrum of contemporary concerns in oncology, with research associated with breast cancer still leading the way. This presentation will provide an integrative context for the papers which are to follow, by summarising progress and highlighting current psychosocial research issues in each of the three key areas represented in the symposium i.e. prevention, treatment research and patient care. The need to consider how psychosocial research findings influence future practice in these domains will be discussed.

560 ORAL

Does psychological response influence survival from breast cancer?

M. Watson[1,2], J.S. Haviland[2], S. Greer, J. Davidson[2], J.M. Bliss[2]. [1]*The Royal Marsden Hospital;* [2]*Institute of Cancer Research, London and Sutton, UK*

Purpose: To clarify the impact of psychological response on survival of a large cohort of women with early breast cancer.

Method: 578 women were enrolled into a prospective survival study. Psychological response was measured using the Mental Adjustment to Cancer (MAC) Scale, the Courtauld Emotional Control Scale (CECS), the Hospital Anxiety and Depression Scale (HADS) assessed between 4–12 weeks post-diagnosis. Cox proportional hazards regression was used to obtain the hazard ratios for the measures of psychological morbidity, adjusting for a number of prognostic factors associated with survival.

Results: At 5 years 392 were alive and without relapse, 50 alive with relapse and 133 had died. There was a suggestion of increased risks of death from all causes by 5 years in women with high scores on MAC helplessness and HADS depression, although only the result for HADS depression reached statistical significance. When adjusting for all prognostic factors and all MAC and HADS scores, the effect of HADS depression was no longer significant. For event-free survival there was a significant increased risk of cancer death or relapse by 5 years in women with high scores on MAC helplessness. This remained significant after adjusting for all prognostic factors and all MAC and HADS scores (HR = 1.63, 95% CI 1.07–2.49, for a MAC helplessness score of $\geq$12).

Conclusion: For overall survival there is a borderline effect of MAC helplessness, but a high score for HADS depression results in a significantly worse survival. For 5 year event free survival a high MAC helplessness score has a significant detrimental effect.

561 ORAL

Depression subsequent to breast cancer

K. Hjerl[1], E. Olsen[2], N. Keiding[2], P.B. Mortensen[3], T. Jørgensen[1]. [1]*Centre of Preventive Medicine, KAS Glostrup;* [2]*Department of Biostatistics University of Copenhagen;* [3]*Department of Psychiatric Demography, University Hospital of Århus, Denmark*

Purpose: To test the hypothesis that women subsequent to invasive primary breast cancer have an increased risk of admission into psychiatric departments with affective or neurotic disorders.

Method: The base population comprised all 64,927 women registered in the nation-wide Danish Cancer Registry with primary invasive breast cancer during the period 1970–1993. By cross-linkage to the nation-wide Danish Psychiatric Central Register we identified women admitted with an affective or neurotic disorder subsequent to breast cancer.

The incidence of admission into psychiatric department with affective or neurotic disorder in women with breast cancer is compared to the incidence of admission into psychiatric department with affective or neurotic in the normal population of women adjusted for age, calendar period and urbanity.

Results: Women with breast cancer have an significant increased risk of admission into psychiatric department with affective or neurotic disorders in a period in connection with the diagnosis of breast cancer. The timedependent incidence rates will be presented.

Conclusion: Breast cancer seems to be a risk factor for admission into psychiatric departments with affective and neurotic disorders.

562 ORAL

Psychosocial implications of prophylactic bilateral mastectomy

M.B. Hatcher, L.J. Fallowfield, K. Thirlaway, A. Hall. *CRC Psychosocial Oncology Group, Dept of Oncology, University College London, UK*

Purpose: With the numbers of women contemplating prophylactic bilateral mastectomy increasing it is important that the psychological costs and benefits of this procedure are established.

Method: The study will measure psychological morbidity, describe the decision making process, determine the communication and counselling needs and identify pre-operative factors that may predict post-operative distress. 76 women will be interviewed before surgery, then at 6 and 18 months post operatively. 76 women declining surgery will be interviewed after first contact, then 18 months later. All women will be given standard psychological questionnaires to complete at each interview.

Results: Interim analysis shows that women opting for surgery have a more accurate perception of the general population risk, but when it comes to personal risk estimates a higher percentage of the surgical group felt it was inevitable that they would develop the disease. Analysis of the General Health Questionnaire, a screening tool for psychiatric distress, has shown that women opting for surgery are also more distressed than those opting for regular surveillance. A strong factor that appears to be associated with those opting for surgery, and which also appears to influence decision making, is personal family history. Other issues that are emerging include: insufficient information; lack of funding; isolation and post-operative complications.