(ATRA) and compare NIS gene expression to established breast cell lines MCF-7 (breast cancer) and MCF-10A (normal breast).

Material and methods: Cells for primary culture were obtained from human tumors and surrounding tissues, excised routinely during mastectomy, fragmented, digested and purified by lymphocyte and fibroblast depletion. Cells were cultured for 2-5 days and stimulated by ATRA (12 hours, 1 micromole/L). NIS expression was quantified by real-time PCR. Simultaneously, analysis in MCF-7 and MCF-10A cell lines was performed, we also compared the obtained NIS expression to a panel of 5 papillary thyroid cancer tissues, which exhibited iodine uptake.

Results: The mean basal NIS expression in analyzed breast cancer specimens was approximately 74% of the level observed in MCF-7 cell line. In 5 cases, where we obtained growth of normal breast cells, the basal NIS expression was lower than in tumor tissue, mean NIS expression in those cells was 86% percent of the level in MCF-10A cell line. After stimulation with ATRA, 3 of 12 tumors (25%) exhibited pronounced increase in NIS expression, up to 55%, 44.1% and 20.9% of NIS expression in MCF-7 stimulated cells. This level of expression was approx. 27% of value observed in a panel of papillary thyroid ca. Stimulation of normal breast tissue with ATRA did not induce increase of NIS expression above the level in MCF-10A stimulated cells.

Conclusion: There is basal low-level NIS expression in analyzed breast cancer primary cultures, reaching 74% of expression in MCF-7 line. This low-level expression could be further stimulated in certain cases, with NIS expression comparable to the level observed in tissues exhibiting iodide uptake sufficient for therapy.

392 POSTER

Stage and survival in breast cancer in Estonia: the EUROCARE high-resolution study

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EUROCARE-2 study revealed low survival rate of brest cancer (BC) patients in Estonia compared to the more affluent European countries: the age-standardised 5-year relative survival rate was 60% in Estonia in 1985-1989 (the weighted European average 73%). To find out the reason for the differences, the EUROCARE-2 High-Resolution Study was carried out. Purpose. The aim of our study was to evaluate the stadge distribution, diagnostic and treatment methods, and survival of the BC patients in Estonia.

Material and Methods: 224 BC cases, diagnosed and treated in the area of the Estonian Cancer Centre between 01.01 and 31.08.1991, were included. The case selection based on the Estonian Cancer Registry. Patients were followed-up until 31.12.1996. Clinical data were retrospectively collected by the EUROCARE protocol.

Results: The median age of patients was 59 (range 30-95). The diagnose was proved by histology in 76% and by cytology in 21% of patients. The stadge distribution of cases according to TNM: Stage I – 8%, stage II – 51%, stage III – 22% and stage IV 8%; the stage was not determined for 11% of patients. Surgical treatment was performed for 75% of patients. From those, mastectomy by Madden was made for 77%, by Halstead for 14% and simple mastectomy for 10% of the patients. The axillar lymphadenectomy was performed in 71% of patients. The chemotherapy was given to 47% of patients (21% in stage I, 41% in stage II, 71% in stage III and 76% in stage IV). The radiotherapy was performed in 32% of patients, and hormonal therapy was used in 77% of patients. The 5-year relative survival was 64% and varied by stage (97% in stage I, 83% in stage II, 48% in stage III and only 12% in stage IV).

Conclusion: The survival of patients with BC diagnosed inEstonia in 1991 has been slightly increased, compared to the EUROCARE-2 period (1985-1989). However, the proportion of small tumours (T1N0M0) was lower, and the proportion of advanced tumours was higher in Estonia than in many other European countries.

393 POSTER

Effect of anastrozole therapy on bone: preliminary results of digital radiometrical analysis of clavicle and rib.

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Background: Anastrozole (ANS) is a potent aromatase inhibitor used in the treatment of advanced breast cancer (BC) and being investigated as an adjuvant or chemopreventive agent. The concerns exist that ANS as a potent estrogen suppressor may increase the risk of disorders related to hypoestrogenemia, such as reduction in bone mass.

Material and methods: Estimation of ANS effects in skeleton was performed using the modified method of radiometrical digital analysis of clavicle and II-nd rib described before (*Breast Cancer Res Treat* 2002;73,189). We report pilot results obtained from 20 women with ER/PR-positive or ER/PR-unknown BC (median age: 64 yrs, range: 55-80) being postmenopausal for 5-26 yrs (median: 15). All the patients previously received tamoxifen (median: 24 months, range: 5-60) in adjuvant setting (N=15) or for advanced disease (N=5) and were converted to ANS due to cancer progression (N=17) or tamoxifen-related side-effects (N=3). The radiometry of clavicle and rib was done on routine chest P-A radiograms taken in each patient before and at least 6 months of ANS treatment afterwards (median: 12, range: 7-27) and digitally processed using image analyser. The quantitative analysis was performed in the digital profiles of grey levels plotted perpendicularly to the axis of the bone shadow.

Results: The comparative analysis of the pairs of radiometric data taken before and after treatment reveals that the linear spongious/cortical width ratio (S/C) increases significantly after ANS treatment. Another typical features observed after ANS were the increase of the contrast between cortical and spongious part of bone shadow as well as the increase of coefficient of variance (CV) of grey levels profile. All the above mentioned phenomena were observed in clavicle and rib profiles (Table).

	Clavicle				II-nd rib			
	mean (before ANS)	mean (after ANS)	t-Student for pairs (p)	sign test (p)	mean (before ANS)	mean (after ANS)	t-Student for pairs (p)	sign test (p)
CV	8.23%	9.20%	0.40	0.18	10.78%	11.52%	0.61	0.61
contrast	1.13	1.15	0.49	0.42	1.18	1.22	0.45	0.12
S/C	0.53	0.59	0.0006	0.0005	0.61	0.67	0.01	0.12

Conclusion: The radiometric data suggests that ANS therapy enhance the radiological signs of bone mass loss. The study is going on and the updated results will be presented at the conference.

394 POSTER

Survival and quality of life in breast cancer patients

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This was a prospective investigation to study the contribution of quality of life in relation to survival in breast cancer patients. In all, 128 breast cancer patients were followed up for five years. At five years 79 patients were alive and 49 patients were dead, given an overall survival rate of 62%. Quality of life was measured using the EORTC QLQ-C30 and its breast cancer questionnaire (QLQ-BR23) after completion of the initial treatment. Data for 116 patients were available for analysis. Of these, 44 patients presented with metastatic disease, and 95 patients went under mastectomy. Using the Cox regression model after adjusting for age at diagnosis and the disease stage, the results showed that receiving neo-adjuvant therapy as initial treatment and the lower global quality of life were independent predictors of poorer survival (Hazard ratio for neo-adjuvant therapy = 12.4, 95% CI = 4.9 to 31.0, P

395 POSTER

Is health insurance coverage a major determinant of breast cancer screening practice?

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Breast cancer screening practice (BCS) is a helpful measure to reduce breast malignancies morbidity and mortality. However BCS rates in Greece are not satisfactory. Considering the cost of early diagnostic procedures, the presence and type of health insurance may constitute an important determinant of screening practice.

Purpose of the study: To evaluate if patientsí health insurance coverage plays a role on BCS.

Material and methods: 1420 women (aged 40-80) insured by 4 major Hellenic health insurance companies were included in the study: 505 were insured by the Institute of Social Insurances (IKA), 549 by Agricultural Insurances (OGA), 260 by Public Insurance (DHM), and 106 by Trade and Craftsmanship's Greek fund = (TEBE). Women without health insurance coverage were used as a control group (Contr). The annual screening rates by means of clinical breast examination (CBE) and mammogram (MRX) were analyzed. For the subgroup of women aged 40-49 BCS practice was analyzed within a period of two years.

Results:

Age	Test	Contr	IKA	OGA	DHM	TEBE
40-49	CBE	26,0%	47,2%	38,2%	49,5%	36,1%
50-59	CBE	11,1%	27,9%	13,0%	27,3%	28,5%
60-69	CBE	9,0%	13,1%	10,5%	14,2%	10,3%
70-80	CBE	0%	11,6%	4,7%	6,6%	14,2%
40-49	MRX	20,0%	26,7%	23,4%	34,1%	27%
50-59	MRX	0%	22,0%	11,5%	17,8%	14,2%
60-69	MRX	9%	9,6%	10,0%	16,3%	3,4%
70-80	MRX	0%	13%	4,7%	6,0%	-

Conclusion: Health insurance coverage plays a main role in BCS practice. In all the age-subgroups analyzed women without health insurance showed the lowest rate both for mammography and clinical breast examination. However BCS practice did not exceed the 50% in any of the investigated subgroups.

Breast cancer adjuvant therapy

396 POSTER

Randomized controlled study comparing surgery alone, surgery plus tamoxifen, and surgery plus tegafur-uracil in patients with node-negative breast cancer: 5-year results from the Kanto cooperative study group of adjuvant chemo-endocrine therapy for breast cancer (ACETBC) of Japan

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Background: Development of highly convenient and safe postoperative adjuvant therapy is awaited specially for the patients with breast cancer without lymph node metastasis but with poor prognosis. We performed a randomized controlled study in Japanese women with node-negative breast cancer to compare the outcome of the three groups of patients assigned to surgery alone, or postoperative adjuvant therapy with tamoxifen, or surgery plus the oral 5-fluorouracil derivative tegafur-uracil (UFT). We report the results of 5 year follow-up.

Subjects and Methods: Eligible patients comprised women with breast cancer who had undergone mastectomy, had tumors of 5 cm or less in diameter, and had no histological evidence of lymph node metastasis. Enrolled patients were randomly assigned by the minimization method to receive surgery alone (surgery group) or surgery plus tamoxifen (tamoxifen group, 20 mg/day, orally for 2 years) or surgery plus UFT (300 mg/day, orally for 2 years). Treatment response was analyzed on an intention-to-treat basis.

Results: A total of 671 women (surgery group, 223; tamoxifen group, 224; UFT group, 224) were enrolled from 1992 through 1994. The 5-year survival rate was 93.2% in the surgery group and 95.5% in the tamoxifen group (vs. surgery, P = 0.27), as compared with 97.3% (vs. surgery, P = 0.041) in the UFT group. Subgroup analysis confirmed that UFT was very effective in high-risk patients whose tumors were 2 cm or more in diameter (vs. surgery, P = 0.041) or patients for estrogen negative receptor (vs. surgery, P = 0.037).

Conclusions: Our results suggest that postoperative chemotherapy withUFT is effective in women with node-negative breast cancer.

397 POSTER

Preoperative trastuzumab and vinorelbine (HN) is a well-tolerated, active regimen for Her2 3+/FISH+ stage II/III breast cancer.

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Introduction: The combination of Trastuzumab and Vinorelbine (HN) is well tolerated, with high clinical activity (RR 68-78%) in patients with HER2 overexpressing, metastatic breast cancer. To evaluate this regimen in early stage breast cancer, we conducted a phase II study of preoperative HN, followed by breast surgery, and postoperative doxorubicin/cyclophosphamide (AC).

Study Design: The primary endpoint was pathological complete response, defined as absence of invasive cancer. Eligible patients had HER2 3+ by IHC or FISH+ tumors, clinical stage II or III disease (including inflammatory breast cancer), and normal LVEF. Preoperative therapy consisted of trastuzumab (4 mg/kg x 1, then 2 mg/kg weekly x 11) with vinorelbine (25 mg/m^2 weekly x 12). Adjuvant AC at standard doses of 60/600 mg/m^2 respectively, every 3 weeks x 4, was given postoperatively. Higher risk patients subsequently received trastuzumab/paclitaxel; all patients received a total of 52 weeks of trastuzumab. LVEF was assessed at baseline, following HN, after 4 cycles of AC and every 3 months while on protocol-based therapy.

Results: To date, 39 patients with clinical stage II (12/39=31%) or III (27/39=69%) cancer have completed HN>surgery>AC therapy and are currently evaluable for efficacy and safety. Asymptomatic grade 2 cardiac toxicity was seen in 2 patients, following AC therapy. One patient came off study following AC for tachycardia with palpitations. Full dose HN was delivered on 302/324 HN planned weekly doses. A reduced dose of N was administered on 14/324 weeks and N was omitted 8/324 weeks. One patient had grade III stomatitis, and nausea. No other Grade III/IV toxicities were seen during HN. Clinical response (CR+PR) was observed in 36/39 patients (92%). Pathological complete response was observed in 8 of 39 patients (21%). In patients with residual tumor at the time of surgery, 85% had persistent HER2 by immunostaining (3+) or FISH (>2 copies HER2/cell). Correlative studies on HER2 in circulating tumor cells and tissue will be presented.

Conclusions: Neoadjuvant HN is well tolerated in women with stage II/III HER2+ breast cancer, and has significant clinical activity, warranting further exploration in early stage breast cancer. Residual breast cancer remains HER2 positive, suggesting that selection of non-HER2 expressing clones is not a common mechanism of resistance to Herceptin/vinorelbine.

398 POSTER

Self-reported cognitive function appears unimpaired by adjuvant chemotherapy for breast cancer in post-menopausal women.

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Our purpose was to evaluate the possible impact of adjuvant chemotherapy for breast cancer on cognitive and other functional domains of health-related quality of life (HRQL).

Methods. Sixty-five post-menopausal women completed the EORTC QLQ-C30 core HRQL questionnaire, BR23 breast cancer module, and other measures prior to, during, and at the completion of adjuvant chemotherapy, and 6 months later. All patients received 5-fluorouracil, doxorubicin, cyclophosphamide (FAC). Changes in QLQ-C30 functional scale scores of between 5 and 10 are perceived by patients as small, and changes of between 10 and 20 as moderate.

Results. Mean patient age was 60 years (range 31-80). Mean drug dose intensities ranged from 92-94%. Cognitive function did not change significantly from baseline (84 ± 18, mean ± standard deviation) to completion of chemotherapy (80 ± 20, P=0.11). The mean change in CF was -5 ± 19 (95% confidence interval (c.i.) 10 to 1) and was not related to patient age or drug dose intensity. By contrast, physical function, role function, social function and global health status decreased and fatigue increased during chemotherapy (all P<0.01). Mean changes in physical