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

function (-14 ± 19, 95% c.i. 8 to -19) and role function (-18 ± 22, 95% c.i. -11 to -24) were moderate in clinical magnitude. Emotional function was better at the completion of chemotherapy than baseline (P<0.01). At six months after completion of chemotherapy, cognitive function (83 ± 24), physical function, role function and global health status did not differ from baseline values.

Conclusions. We conclude that (1) self-reported cognitive function is unimpaired or impaired to a minor extent by adjuvant chemotherapy for breast cancer, (2) whereas physical function and role function are impaired to a moderate extent by adjuvant chemotherapy, but recover subsequently. These data are longitudinal and avoid potential confounding by the effects of chemotherapy-induced menopause; however, the instrument does not address specific cognitive domains in detail and may be insufficiently sensitive to limited but clinically relevant changes in cognitive function.

399 POSTER

Cost-effectiveness of intensive adjuvant chemotherapy for high-risk breast cancer: Is dose-escalated chemotherapy with growth factor support (GFS) more costly and less effective than high dose chemotherapy (HDCT) with peripheral stem cell transplantation (PSCT)?

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Background: Based on randomized studies HDCT with PSCT is not superior to conventional CT as adjuvant treatment for high-risk breast cancer patients. The cost-effectiveness of these treatments has never been compared. In the present study, we examined the actual treatment costs of Finnish high-risk breast cancer patients treated with adjuvant chemotherapy in the Scandinavian Breast Cancer Group Adjuvant Trial, SBG9401 (Bergh et al. Lancet 2000;536,1384).

Patients and methods: Fifty-nine patients were randomized to nine cycles of dose escalated FEC (5-fluorouracil-epiadriamycin-cyclophosphamide) with granulocyte GFS (group A) and seventy patients to three cycles of standard FEC and HDCT with PSCT (group B). Both groups received adjuvant radiotherapy and tamoxifen for five years. All treatment costs (hospitalization, drugs, transfusions, growth factors etc) were considered. Effectiveness was measured by the number of days on sick leave and survival. Two patients did not receive the trial medication and were excluded. The mean age of the patients at the time of diagnosis was 49 years (range 41-59 yrs, N.S.)

Results: The mean total costs of the adjuvant treatment were significantly higher in group B (25829 * vs. 36605 *, p < 0.05). The main reason for the higher costs was the higher amount of hospitalization days. The lowest total cost (22047 *) for an individual patient occurred in group A and the highest (52451 *) was recorded in group B. Costs of filgrastim were 15335 * in group A and 2969 * in B. The costs of radiotherapy were almost similar in both groups: 1687 * in A (6% of total costs) and 1573 * in B (4% of total costs). Surprisingly there was no difference (p=0.5) in the number of sick leave days between the groups, mean 435 days. At 35 months' follow-up 88% patients in group A and 80% in group B were alive (N.S.).

Conclusions: The HDCT with PSCT (group B) was significantly more costly than dose escalated FEC with growth factor support (group A) although over half of the total costs in group A were due to growth factors. Radiotherapy was cheap compared to the overall costs (less than 10%). There was no difference between the groups in effectiveness as measured by the number of days on sick leave and survival. According to the SBG9401 and this study HDCT with PSCT as an adjuvant treatment of breast cancer is more costly, but no more effective than dose escalated FEC.

400 POSTER

Dose-dense sequential adriamycin-paclitaxel-cyclophosphamide (A-T-C) chemotherapy in high-risk early breast cancer - a phase II study

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The superiority of dose-dense sequential chemotherapy over conventionally scheduled combination chemotherapy in regard of higher efficiency and less severe toxicity was recently suggested. Fifty patients after surgery for high-risk breast cancer were recruited into a phase II study. The median age was 50 years, the median number of positive nodes was 7, and 10 or more positive nodes were present in 36%. Forty-five percent of the tumors were ER-positive, while 40% were PR-positive. The following chemotherapy schedule was used: 4xA→ 4xT→ 4xC, q2weeks (A = adriamycin 60 mg/m^2, T= paclitaxel 200 mg/m^2 over 3 hours, C= cyclophosphamide 800 mg/m^2). Hemopoietic cytokin was used individually: in the event of neutropenia hampering the implementation of the dose-dense schedule, filgrastim was started and administered in all the subsequent cycles.

Toxicity in dose-dense sequential A-T-C chemotherapy

	Toxicity (% of cycles					
	Adriamycin 1-4		Taxol 1-4		Cytoxan 1-4	
Grade	1-2	3-4	1-2	3-4	1-2	3-4
Nausea	76.1	2.2	11.9	–	62.1	–
Vomiting	23.4	1.4	–	–	29.7	2.7
Neutropenia	25.5	68	61.9	14.3	51.3	10.8
Anemia	79.4	2.1	100	–	97.3	–
Thrombopenia	8.5	–	2.3	–	–	–
Arthralgia	4.3	–	71.5	21.4	–	–
Myalgia	2.1	–	14.2	4.7	–	–
Sensory neuropathy	2.1	–	57.1	–	–	–
Skin	2.1	–	9.5	2.3	4	–

Neutropenic fever occurred 3 times each after treatment with A or T. Grade 2-3 alopecia was usual. Almost all the premenopausal patients developed amenorrhea. A mild and transitory PFS deterioration occurred in 6 patients. Chemotherapy was terminated in 4 cases due to cardiac (A, n=1) or skin toxicity (T, n=1 and C, n=1), or because of an anaphylactic reaction to T (n=1). No cardiac dysfunction was detected. The effective dose intensity was 93.7, 98.1, and 96.6% of that planned in the A, T, and C cycles, respectively. Filgrastim was used in 59.6, 84 and 71.4% of all the A T and C cycles, respectively. Dose-dense sequential A-T-C chemotherapy is well tolerated. Individually used hemopoietic citokines help to maintain the planned dose intensity. The follow-up of the patients, and analysis of the prognostic and predictive factors are planned.

401 POSTER

Adjuvant chemotherapy in breast cancer patients older than 70: CMF or FEC, feasability, acute and late toxicities. Experience of a single Institution

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Background: Breast cancer (BC) in patients older than 70 will be a major health care problem in the next decades. Adjuvant treatment are still not standardized: benefit of chemotherapy seems to exist in regards of age but its toxicities have never been clearly evaluated. Since 2000 in our institution, we used standard prognosis criteria (N+ or size and grade, RH-) for surgery, chemotherapy (CT) and radiotherapy in elderlys. CT was CMF, FEC75 or FEC100. Our aim was to investigate compliance of treatment, toxicities with each regimen.

Patients: We recorded all patients aged 70 or older who underwent adjuvant CT from 2000 to 2002 for BC. Treatment disruption, reasons, acute and delayed toxicities, use of GCSF or erythropoietin (Epo) were reviewed.

Results: There were 95 patients. Median age 75 [70-85]. 5 had inflammatory BC and received primary CT. 57 had a conservative surgery and 36 had a mastectomy. CT was: CMF (60 pts), FEC75 (11pts), FEC100 (17pts). 6 disrupted CT (CMF: 2, FEC75 4). Reasons were fever or asthenia. Any of pts receiving FEC100 stopped CT. In 2002 only one patient disrupted treatment. All but one pt receiving FEC75 had primary preventive GCSF, 5 had curative Epo. All pts receiving FEC100 had GCSF and Epo. All but two grade III and IV toxicities were observed in pts receiving anthracycline: 18 pts had severe side effects: febrile neutropenia (n:9), pulmonary embolism (n: 2), angor (n: 1), 3 pts requiered red blood cell transfusion. Median decrease in Hb is 1.6g/dl with CMF and 2.6 with FEC. Analysis according regimen and comparison with pts youngers, prognostic factors will be analyzed in may 2003. Delayed cardiac toxicity has never been reported.

Conclusions: Adjuvant anthracycline based CT is feasible in elderly with reasonable safety profile but required adequate supportive care. Our data suggest that compliance is influenced by initial criteria and willingness of physician. Factors impacting on toxicity, physician's decisions and compliance of CT will be presented in may.