breast cancer, early

DISTANT RECURRENCES AT MEDIAN OF 5-YEARS AMONG 9,779 POSTMENOPAUSAL WOMEN WITH HORMONE-RECEPTOR-POSITIVE EARLY BREAST CANCER TREATED ON THE TEAM TRIAL OF ADJUVANT ENDOCRINE THERAPY

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Background: The TEAM (Tamoxifen Exemestane Adjuvant Multinational) trial is a multinational study of the effects of 5 years of adjuvant endocrine therapy, either exemestane (E) or the sequence of tamoxifen followed by E (T—E) in postmenopausal early breast cancer. The 5-year results showed no difference in disease-free survival between both arms (Rea, SABCS 2009). The present analysis explores the sites of first reported distant recurrences (DR).

Methods: Between 2001 and January 2006, 9,779 postmenopausal women with hormone-receptor-positive early breast cancer were randomized to E or T—E for 5 years after completion of locoregional therapy with or without adjuvant chemotherapy and/or mastectomy, 68% received radiotherapy, and 36% received chemotherapy. Thirteen patients withdrew consent.

Results: Based on an intention-to-treat analysis, among 9,766 patients 420 DR occurred in patients randomized to T—E and 400 DR in E (Table). At 5 years cumulative incidence of DR was 8.9% in T—E and 8.4% in E (hazard ratio for E: 1.93; 95% confidence interval 0.81–1.07; p-value 0.31). Table: Sites of 1st reported DR

<table>
<thead>
<tr>
<th>Mode</th>
<th>T—E arm (468)</th>
<th>E arm (489)</th>
</tr>
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<td>Bone only (1)</td>
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<td>116 (24%)</td>
</tr>
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<td>Visceral only (2)</td>
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<tr>
<td>Overall</td>
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</table>

(1) i.e. not visceral; (2) i.e. not bone; (3) includes soft tissue and nodes.

Conclusions: This explorative analysis showed that there is no difference in time to DR between upfront E and sequence of T—E. In addition the site of the first reported DR is not significantly different between both arms. As such, both regimens are appropriate treatment options for postmenopausal women with hormone-receptor-positive early breast cancer.

Disclosure: D. Rea is the recipient of a research grant from Pfizer. He has also disclosed that he is on the speaker’s bureau for AstraZeneca and Novartis. He has also disclosed that he is a consultant for Pfizer AstraZeneca and Novartis. C. Markopoulos received research grants and honoraria for lectures from AstraZeneca, Novartis, and Pfizer. S. Jones has disclosed that he is on the speaker’s bureau for Pfizer USA. He has also disclosed that he is a consultant for Pfizer. All other authors have declared no conflicts of interest.

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FINAL RESULTS OF THE HELLENIC COOPERATIVE ONCOLOGY GROUP PHASE III TRIAL (HE-1000) EXPLORING THE EFFICACY OF POSTOPERATIVE DOSE-DENSE SEQUENTIAL CHEMOTHERAPY WITH EPIRUBICIN, PACLITAXEL AND CMF IN HIGH RISK BREAST CANCER PATIENTS

Data Office, Hellenic Cooperative Oncology Group (HeCOG), Athens/GREECE

Background: To explore the impact of Dose Intensity (DI) in the adjuvant setting of Breast Cancer, a randomized phase III trial was conducted comparing postoperative dose-dense sequential chemotherapy with epirubicin, paclitaxel and CMF in high risk breast cancer patients.

Patients and methods: From October 2000 to June 2005, 1,121 node-positive patients were randomized to dose-dense sequential epirubicin 110 mg/m2 and paclitaxel (Taxol®; Bristol Myers-Squibb, Princeton, New Jersey, USA) 250 mg/m2 (group A), or concurrent epirubicin 83 mg/m² and paclitaxel 187 mg/m² (group B), both followed by three cycles of ‘intensified’ combination chemotherapy with cyclophosphamide, methotrexate and fluorouracil (CMF). By protocol design total cumulative dose and duration of treatment were identical in both groups. Dose intensity of epirubicin and paclitaxel was double in the dose dense arm. Prophylactic treatment with granulocyte colony-stimulating factor was given with the dose-dense treatments. Disease-free survival (DFS) was the primary endpoint.

Results: At a median follow-up of 76 months, 305 DFS events (155, group A and 152, group B) and 208 deaths (101, group A and 107, group B) have been observed. The 5-year DFS rate of 74% and 74% and OS rate of 86% and 85% were observed for group A and group B respectively. No differences were found in DFS or OS between the two treatment groups (p=0.78 and p=0.58 for DFS and OS respectively). Safety analysis showed that both regimens were well tolerated and safe have been previously published (Fountzilas et al. Ann Oncol 2008).

Conclusion: No DFS or OS benefit from the dose-dense sequential epirubicin and paclitaxel was detected when compared to the concurrent administration of the same drugs.

Disclosure: G. Fountzilas: On behalf of the Hellenic Cooperative Oncology Group (HeCOG) Prof. G. Fountzilas has pending patent application with Siemens Healthcare Diagnostics, Cologne, Germany. All other authors have declared no conflicts of interest.

HER2 STATUS AS PREDICTOR OF MAMMOGRAPHIC SCREENING DETECTION: COMPARISON OF INTERVAL- AND SCREEN-DETECTED BREAST CANCERS

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Introduction: To determine whether markers of poor prognosis are associated with risk of breast cancer diagnosis in the interval between screening examinations, we estimated the effect of the mode of detection on distribution of breast cancer molecular subtypes using population cancer registry data.

Materials and methods: Subjects (n = 641) comprised all breast cancers systematically collected by the Cancer Registry of Parma Province and diagnosed in women aged 50-69, from 2004 to 2007. These included 370 screen-detected and 271 symptomatic breast cancers (63 women with screen-detected cancers who had not attended screening). We used logistic regression to determine whether interval cancers were associated with selected clinical and biologic characteristics. We also estimated the relative risk of cause-specific fatality and disease-free survival (DFS) by each resulting predictive factor (screen-detected compared to either symptomatic or interval cancers).

Results: Interval-detected cancers occurred more in younger women and were of more advanced tumor stage than screen-detected cancers. In unconditional logistic regression models adjusted for age and tumor stage, tumors with high histologic grade (odds ratio[OR] = 2.2; 95% CI =1.0–5.4), high proliferation rate (OR =2.7; 95% CI =1.5–4.8), or positive HER2 status (OR =2.6; 95% CI =1.3–5.1) were more likely to surface in the interval between screening examinations. After adjusting for various potential biases, women with screen-detected breast cancer had a substantial survival advantage over those with symptomatic breast cancer. In a multivariate model, positive HER2 status independently predicted poor DFS when the mode of
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cancer detection was included as covariate in addition to age, histologic grade, proliferation rate, and tumor stage.

Conclusions: This is the first population-based cancer registry study demonstrating that HER2-positive tumors account for a substantial proportion of mammographic screening failure to detect breast cancer. Our data indicate that molecular subtype distribution of screen-detected breast cancer differs from that of interval cancers and accounts in part for the better outcome of screen-detected cancer.

Disclosure: All authors have declared no conflicts of interest.

218PD ABCSG-24: EFFICACY OF ANTHRACYLINE- AND TAXANE-BASED NEOADJUVANT THERAPY + CAPECITABINE (C) IN TRIPLE-NEGATIVE EARLY BREAST CANCER (TNBC)

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Background: In the ABCSG-24 randomised, phase III trial we previously showed that the integration of C into a standard epirubicin and docetaxel (ED) neoadjuvant regimen significantly improves pCR rate (24.3% vs 16.0%; p=0.02; [Steger G, et al. Eur J Cancer Suppls 2009;7:3(Abst 4BA)]. Here we assess whether the addition of C into a standard ED neoadjuvant therapy achieves a significant pCR benefit in patients with TNBC who represent a difficult-to-treat subgroup.

Methods: Patients with biopsy proven operable breast cancer, except T4d, were included in the ABCSG-24 trial. Tumors were centrally reviewed. Tumors were classified into TNBC, non-TNBC and node-positive (N+) based on the ARQ based on the 2000 WHO criteria. Tumor grade was determined by the Scarff-Bloom-Richardson system. Patients were randomised (1:1:1) to receive either ED (31.2%), EDC (39.3%) or EDC/ED (38.1%) for node-negative (N–) and node-positive (N+) tumors.

Results: 512 pts are eligible for safety and efficacy assessment (257 ED; 255 EDC). Addition of C to ED was associated with higher but manageable toxicity. Logistic regression analysis confirmed that patients with TNBC had a significantly greater chance of achieving a pCR than non-TNBC (odds ratio [OR] 5.29, 95% CI 3.22-8.68; p<0.0001). There was no difference in pCR of 16% (EDxT) vs 27% (EDCxT).

Conclusions: Integration of C into standard ED neoadjuvant therapy achieves a significant pCR benefit in patients with TNBC who represent a difficult-to-treat group with the highest unmet therapeutic needs. Patients with non-TNBC also achieved benefit from EDC therapy.

Disclosure: R. Greil: Corporate sponsored research from Roche, not related to breast cancer. B. Milneritsch: Participation in advisory boards for AstraZeneca and Amgen. A. Lang: Dr. Lang received an unrestricted research grant from Jansen Cilag. C. Singer: Amgen research grant received. 10,000 Euro / 3 years. M. Gnant, On behalf of The Austrian Breast and Colorectal Cancer Study Group (abog): Research support from and serving as a consultant for AstraZeneca, Novartis, Roche, Sanofi-Aventis, Schering, Aymen, and Pfizer. R. Greil: Corporate sponsored research from Roche, not related to breast cancer. B. Milneritsch: Participation in advisory boards for AstraZeneca and Amgen. A. Lang: Dr. Lang received an unrestricted research grant from Jansen Cilag. C. Singer: Amgen research grant received. 10,000 Euro / 3 years. M. Gnant, On behalf of The Austrian Breast and Colorectal Cancer Study Group (abog): Research support from and serving as a consultant for AstraZeneca, Novartis, Roche, Sanofi-Aventis, Schering, Aymen, and Pfizer. Other authors have declared no conflicts of interest.

218PD THE DEVELOPMENT OF A FORMULATION OF TRASTUZUMAB FOR SUBCUTANEOUS ADMINISTRATION

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1Christchurch Clinical Studies Trust, Christchurch/New ZEALAND, 2Auckland Clinical Studies Ltd., Auckland/New ZEALAND, 3Clinical Pharmacy, F. Hoffmann-La Roche Ltd, Basel/SWITZERLAND, 4MMSH, F. Hoffmann-La Roche Ltd, Basel/SWITZERLAND

Trastuzumab has been shown to improve disease-free and overall survival in patients with HER2-positive early-stage breast cancer (BC). Standard trastuzumab treatment requires 18–25 infusions over 1 year after chemotherapy and can result in discomfort, inconvenience and a significant time commitment for both health care providers and patients. Subcutaneous administration could significantly simplify treatment, shortening administration and improving patient experience. Recombinant human hyaluronidase (4HuP12) has been developed and approved to improve dispersion and absorption of co-administered drugs. It has been combined with trastuzumab to
allow injection volumes 23 mL to be safely and comfortably administered subcutaneously. The aim of the Phase Ib study were to select the dose of the new subcutaneous trastuzumab formulation with HLA-P402 having comparable exposure to intravenous (IV) trastuzumab and to assess its safety and tolerability in male volunteers and HER2-positive BC patients. Three groups of 6 volunteers received subcutaneous doses of 6, 8 and 10 mg/kg, and 40 patients who had previously received trastuzumab received subcutaneous doses of 8 mg/kg or 12 mg/kg. Doses were delivered through a 27-gauge needle at approximately 2 mL/minute. Controls were 6 male volunteers and 6 patients who received the approved mg/kg IV maintenance dose. The 8 mg/kg dose of the subcutaneous trastuzumab resulted in a Cmax and AUC in the range of the approved 6 mg/kg IV dose in both male subjects and HER2-positive patients. The formulation was well tolerated, with no apparent increase in incidence of adverse events (AEs) with increasing dose. The majority of AEs (72%) were mild. The most common AEs were headache, musculoskeletal pain, diarrhea, nausea, fatigue, and injection site reactions which included discoloration, erythema, and mild discomfort. The total volume administered varied between 3.4-11.9 mL. Subcutaneous trastuzumab can be delivered comfortably and safely while achieving serum exposure comparable to the approved IV formulation in male volunteers and HER2-positive BC patients. The patient experience was favorable. These results support further testing of subcutaneous trastuzumab.

Discussion: C. McIntyre and B. Bittner: is an employee of F. Hoffmann-La Roche Ltd. All other authors have declared no conflicts of interest.

## 219PD
### NEO-ADJUVANT CHEMOTHERAPY TREATMENT AND RESPONSE IN DIFFERENT BREAST CANCER SUBTYPES: POOLED MULTI-LAYER ANALYSIS OF THE GERMAN TRIALS

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Methods: Data from 8 German neo-adjuvant chemotherapy trials with 6625 patients with uniform protocol and outcome definitions were collected between 1998 and 2006 with pathological complete response (pCR) as primary endpoint. The analysis included data from 3332 patients of 7 trials and 12 treatment arms with complete baseline parameters and no confounding by treatment between trials in pCR. The analysis included data from 3332 patients of 7 trials and 12 treatment arms with complete baseline parameters and no confounding by treatment between trials in pCR. The analysis included data from 3332 patients of 7 trials and 12 treatment arms with complete baseline parameters and no confounding by treatment between trials in pCR.

Results: pCR was associated with more cycles (odds ratio [OR] 1.2 with every two additional cycles; p=0.009), with regimens using higher cumulative anthracycline dose effect was pronounced in HER2-negative tumors (OR 1.61), as compared with HER2-positive tumors (OR 0.83; p for interaction p=0.14). There was no evidence that the effect of taxane dose (p for interaction **p=0.022**). Concurrent trastuzumab in patients with HER2-positive tumors increased the odds of pCR 3.2-fold (p<0.001). The association of pCR with increase in cycle numbers was more pronounced in hormone receptor (HR)-positive tumors (OR 1.35) than in HR-negative tumors (OR 1.04; p for interaction **p=0.046**). The anthracycline dose effect was pronounced in HER2-negative tumors (OR 1.61), as compared with HER2-positive tumors (OR 0.83; p for interaction **p=0.14**). There was no evidence that the effect of taxane dose (p for interaction **p=0.64**). The effect of capcitabine (p for interaction **p=0.57**) varied between subtypes. pCR was not different after 4, 8 or 12 trastuzumab cycles (OR per 4 cycles increase 0.97, p=0.87) overall or in subgroups.

Conclusions: HR-positive tumors benefit more from longer neoadjuvant treatments, HER2-negative tumors more from higher anthracyline doses, triple negative tumors from short-term higher dose taxane and anthracyline based treatment. HER2-positive tumors had a substantial benefit from a limited number of at least 4 trastuzumab cycles, and all subtypes had a benefit from the addition of capcitabine.

Disclosure: All authors have declared no conflicts of interest.

## 220PD
### A PRESURGICAL TREATMENT OF LAPATINIB VersUS Placebo in HER-2 POSITIVE BREAST CANCER

A. Decensi1, M. Purtoni1, G. Pruneri2, M. Laazrini1, D. Serrano3, A. Decensi1, M. Purtoni1, G. Pruneri2, M. Laazrini1, D. Serrano3, E. A. Johnson4, O. Pak1, A. Luini2, C. Marriën4, B. Bonneterre5

Methods: We conducted a placebo-controlled trial of lapatinib, a dual HER tyrosine kinase inhibitor, administered for 3 weeks for tru-cut biopsy and surgery in 60 women with HER-2 positive breast cancer to assess its activity in hyperplastic, dysplastic and malignant breast tissue.

Results: The mean±SD percent change of Ki-67 after 3 weeks was -9.3±4.2 in the lapatinib arm and -15.1±20.9 in the placebo arm, with a baseline adjusted mean percent reduction of 20.9%, 95% CI 5.6-36.1, p=0.008. Compared with placebo, the decrease in Ki-67 on lapatinib was greater in ER negative than ER positive tumors, -34.8%, 95% CI 61.0 to -8.6 versus -12.3%, 95% CI -31.8 to 7.2, and in cytosolic PTEN overexpressing tumors (p<0.057). In post-treatment surgical specimens, the median (range) Ki-67 LI was 15% (5-55) on lapatinib versus 20% (9-60) on placebo in ductal intratumoralei neoplasia (p=0.06), and 1% (1-7) versus 5% (1-5) (p=0.006) in ductal hyperplasia. The median surgical tumor diameter was 18 mm (11-57) in the lapatinib arm and 24 mm (10-37) in the placebo arm (p=0.009).

Conclusions: Lapatinib given for 3 weeks prior to surgery can decrease malignant, dysplastic and hyperplastic cell proliferation and tumor size in HER-2 positive breast cancer, providing further rationale for its use in the adjuvant and preventive treatment of HER-2 positive breast cancer.

Disclosure: A. Decensi: The study was supported by GlaxoSmithKline S.p.A. C. Marriën: GSK employer. All other authors have declared no conflicts of interest.

## 221PD
### VALIDATION OF PRO_10, A MULTIGENE PROGNOSTIC SIGNATURE, IN PATIENTS (PTS) WITH EARLY, ESTROGEN RECEPTOR POSITIVE (ER+/-) POSTMENOPAUSAL BREAST CANCER (BC)

A.E. Moor1, C. Guevara2, H.J. Altermann3, R. Jagg4, S. Nep5

Methods: We validated this score in pts treated at Berne University Hospital.

Results: 315 pts with operable postmenopausal ER+ BC between 1996 and 2004 were reviewed. Cases had a first relapse of BC within 5 years from diagnosis; controls were relapse-free for at least 5 years. 48 cases were matched 1:1 with controls based on a matching score incorporating N (2 points) and T stage (1), diagnosis; controls were relapse-free for at least 5 years. 48 cases were matched 1:1 with controls based on a matching score incorporating N (2 points) and T stage (1), diagnosis. PRO_10 is considered a match. The prognostic impact of PRO_10 was tested by conditional logistic regression analysis. Kaplan Meier estimates and log rank tests were used for survival analysis.

Discussion: Pts characteristics were typical for the population of postmenopausal patients with BC (median age 64; pt1 37%; pt2 63%; p=0.01-0.14). Prognostic for recurrence of BC in the whole group of patients and in subgroups of grade 2 and N0 cancers. 5 yr recurrence-free survival (RFS) was 29% in pts with high and 67% with low scores (P<0.002); median RFS was 4.0 years with high and not reached with low scores. PRO_10 was prognostic for overall survival (5 year OS 71% vs. 91%, median OS 8.1 years vs not reached, P=0.0057).

Disclosure: PRO_10 was validated in "real life" pts treated in a university hospital after tight matching of clinical parameters in cases and controls. PRO_10 is an independent prognostic marker in postmenopausal ER+ BC which can be implemented easily into routine diagnosis. PRO_10 predicts recurrence: conditional logistic regression analysis.
Purpose: The Oncotype DX 21-gene Recurrence Score (RS) assay quantifies the risk of distant recurrence in hormone-treated patients with lymph node-negative, estrogen receptor-positive breast cancer and predicts magnitude of chemotherapy benefit. U.S. distant recurrence in hormone treated patients with lymph node-negative, estrogen receptor-positive breast cancer, and predicts magnitude of chemotherapy benefit. U.S.

Patients and methods: Patients with lymph node-negative, estrogen receptor-positive, HER2 negative, early-stage breast cancer, without contraindication to hormonal treatment and chemotherapy, were enrolled. Before and after obtaining the Oncotype DX assay, medical oncologists stated their adjuvant treatment recommendation and confidence in it. Results: To date, 92 patients have been recruited and pre- and post-RS recommendations are available from 71 cases; 40 (56.3%) with low RS (<18), 25 (35.2%) with intermediate RS (18-30) and 6 (8.9%) with high RS (>31). Treatment recommendation changed for 20 patients (28%); in 11 (15.5%) patients the shift was from chemotherapy plus hormonal therapy (CHT) to hormone therapy alone (HT) and in 9 (12.7%) from HT to CHT. All patients with low RS received HT and all with high RS received CHT. In the group with intermediate RS, 11 received HT and 14 CHT. The probability of changing the initial recommendation based on the RS was 10% (25/246) in low risk grade, 29.4% (12/41) in intermediate grade, and 43% (6/14) in high grade tumors, suggesting a possible relation between tumor grade and the likelihood of recommendation shift. Tumor grade was not available in 3 tumors. In 47 (66%) cases, the medical oncologist’s confidence in their recommendation increased by assessing RS.

Conclusion: The results support the concept of clinical utility for RS assay on medical oncologist adjuvant treatment recommendations in a GEICAM setting. Acknowledgments: RTICC support, ISCiii, Spain


Background: Approximately 70% of patients (pts) with AxN-BC are cured by loco-regional therapy. For pts with rec+ disease, adjuvant endocrine therapy (ETx) reduces the relapse risk (RR) by approximately 1/3. Adjuvant chemotherapy (CTx) reduces RR another 1/3, and is widely used. Thus 90% of pts may receive unnecessary or futile CTx. The validated Oncotype DX assay (O DX) uses the expression of 21 genes in BC as a prognosticator, dividing pts into high (HR), intermediate (IR) and low risk (LR) groups based on “recurrence scores” (RS) of >30, 18-30 and <18 respectively. HR pts benefit from CTx, whereas LR pts do not benefit from CTx. The data for IR are unclear, and are the subject of the TailorRx Trial (ECOG). While widely used in the USA, there is limited European experience with O DX. We studied the potential economic impact of O DX based on a large single institution European experience.

Methods: The outcomes of 140 pts with AxN-BC were retrospectively analyzed. Treatment and chemotherapy, were enrolled. Before and after obtaining the Oncotype DX assay, medical oncologists stated their adjuvant treatment recommendation and confidence in it. Results: To date, 92 patients have been recruited and pre- and post-RS recommendations are available from 71 cases; 40 (56.3%) with low RS (<18), 25 (35.2%) with intermediate RS (18-30) and 6 (8.9%) with high RS (>31). Treatment recommendation changed for 20 patients (28%); in 11 (15.5%) patients the shift was from chemotherapy plus hormonal therapy (CHT) to hormone therapy alone (HT) and in 9 (12.7%) from HT to CHT. All patients with low RS received HT and all with high RS received CHT. In the group with intermediate RS, 11 received HT and 14 CHT. The probability of changing the initial recommendation based on the RS was 10% (25/246) in low risk grade, 29.4% (12/41) in intermediate grade, and 43% (6/14) in high grade tumors, suggesting a possible relation between tumor grade and the likelihood of recommendation shift. Tumor grade was not available in 3 tumors. In 47 (66%) cases, the medical oncologist’s confidence in their recommendation increased by assessing RS.

Conclusion: The results support the concept of clinical utility for RS assay on medical oncologist adjuvant treatment recommendations in a GEICAM setting. Acknowledgments: RTICC support, ISCiii, Spain

sub-studies of the TEAM trial conducted in Germany, the Netherlands/ Belgium and the United States to determine the effects on bone health.

Methods: Patients were randomised to exemestane or tamoxifen as adjuvant therapy for hormone receptor-positive breast cancer. Bone mineral density (BMD) was assessed by dual-energy X-ray absorptiometry at baseline and after 6, 12 and 24 months' treatment. Bone turnover markers were also measured.

Results: 412 patients were evaluable. Patients in the tamoxifen group showed a mean increase in lumbar spine BMD of 1.2% from baseline to month 12 and 0.2% to month 24. Patients in the exemestane group showed a mean decrease from baseline of 2.6% after 12 months and 3.5% after 24 months. There were significant differences in the changes in BMD at the lumbar spine between treatment groups (p<0.001 at all timepoints). In the exemestane group, a mean decrease in total hip BMD of 0.8% from baseline to month 12 and a mean decrease from baseline of 0.4% after 24 months was observed, compared with a mean decrease of 1.3% after 12 months and 3.3% after 24 months in the exemestane group. Changes in BMD from baseline at the total hip were also significantly different between exemestane and tamoxifen (p<0.05 at both timepoints). Bone turnover markers decreased from baseline with tamoxifen and increased with exemestane.

Conclusions: After 24 months, exemestane treatment resulted in decreases in BMD and increases in bone turnover markers. In contrast, BMD was increased and bone turnover markers were decreased with tamoxifen. BMD and bone turnover changes appeared to stabilise after initial treatment.

Disclosure: All authors have declared no conflicts of interest.

Method: Female breast cancer patients receiving adjuvant care in the US Oncology network over a 36 month period (7/1/06 – 6/30/09) were identified using the iKnowMed (iKM) electronic medical record system. Patients were characterized with respect to HER2 status, trastuzumab utilization, ER/PR status, age, and practice region. HER2 status was determined by FISH or IHC testing. Associations between HER2 status and trastuzumab use and clinical characteristics were evaluated using chi-squared and t-tests.

Results: Overall, HER2 status was available for 80% of patients. Among 26,839 patients with documented HER2 status, 18% (n=4,871) were HER2+; 79% (n=21,128) were HER2- and 3% (n=831) had an inconclusive HER2 status (i.e. HER2 overexpression + by IHC with no subsequent confirmatory HER2 testing documented). Not surprisingly, there was a strong association between HER2 status and trastuzumab utilization (p<0.001). Among 2,647 patients receiving trastuzumab with documented HER2 status, 2,303 (95%) were HER2+ and 63 (7%) had inconclusive HER2 status. Ninety-two percent of actively treated HER2+ patients had received trastuzumab vs. 1% of HER2- patients and 36% of patients with inconclusive HER2 status. Hormonal status was associated with trastuzumab use (25% of ER and/or PR+ patients receiving trastuzumab vs <10%). No age differences were observed between patients receiving trastuzumab and those not receiving trastuzumab.

Conclusion: Results suggest that rates of HER2+ disease in early breast cancer, found to be 18% in this study, may be different (possibly lower) from rates reported in the NEMESI study on early breast cancer (EBC) management.

Disclosure: M. Brammer: I am an employee Genentech, Inc a wholly owned subsidiary of the Roche group, sponsor of this project. I additionally maintain financial interest in the form of stock options for the Roche group. S. Gruschuk: I received funding for execution of this project from Genentech, Inc a wholly owned subsidiary of the Roche group. D. Lalla: I am an employee Genentech, Inc a wholly owned subsidiary of the Roche group, sponsor of this project. I additionally maintain financial interest in the form of stock options for the Roche group. J. Doan: I am an employee Genentech, Inc a wholly owned subsidiary of the Roche group, sponsor of this project. I additionally maintain financial interest in the form of stock options for the Roche group. M. Forsyth: I am an employee of US oncology Inc, which received funding from project sponsor, Genentech, to execute and complete the project.
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**Disclosure:** D. Dondi: Employed at sanofi-aventis as Medical Advisor Oncology. All other authors have declared no conflicts of interest.

**ANTHRACYCLINE AND CONCURRENT RADIOTHERAPY SIGNIFICANTLY REDUCED BREAST CANCER RELAPSE RATE**

**Introduction:** The optimal sequencing of chemotherapy and radiotherapy after breast surgery was largely studied but remains controversial. The aim of our study was to evaluate the efficacy and safety of the concomitant use of anthracycline with radiotherapy. This study is the follow-up of previous investigation.

**Methods:** All patients having operable breast cancer treated by chemotherapy and radiotherapy in concomitant way between January 2001 and December 2003, in our centre were included in this nonrandomized comparative study. The study compares two adjuvant treatments using concurrent chemoradiotherapy, the first with anthracycline group (A) and the second with CMF (B) group.

**Results:** In the two groups (A+B) of patients (n=400; 249 in group A and 151 in group B), and when only the cases of isolated locoregional events were considered, the locoregional recurrence free survival (LRFS) in 5 years was 98.7% in group A and 93.5% in group B (hazard ratio [HR] = 0.238; 95% CI 0.067 to 0.997; log-rank P = .034). In the anthracycline group, the 5 years event free survival (EFS) was 80.4% compared to 75.1% in the CMF group (HR = 0.665; 95% CI, 0.435 to 1.06; log-rank P = .057). The 5 years overall survival (OS) was 82.5% and 79.2% in the anthracycline and CMF groups respectively (HR = 0.708; 95% CI, 0.455 to 1.128; log-rank P = .143).

In multivariate analysis we confirmed the positive effect of anthracycline regimens on EFS (HR = 0.539; 95% CI, 0.344 to 0.846; P = 0.007) and OS (HR = 0.63; 95% CI, 0.401 to 0.991; P = .046). LRs, EFS and OS were significantly higher in the anthracycline group in patients (n=288) receiving ≥2 cycles of concurrent chemotherapy (P = .038, P = .026 and P = .038, respectively). LRs and EFS were significantly higher in the anthracyline group in the breast conservative therapy subgroup (P = .049 and P = .04, respectively).

There were more hematologic, and grade 2 skin toxicity in the anthracyline group.

**Conclusion:** We conclude that the treatment based on anthracycline and concurrent radiotherapy reduced breast cancer relapse rate including locoregional recurrences and significantly improved LRs, EFS and OS for the patients receiving ≥2 cycles of concurrent chemotherapy. Concurrent use of anthracycline was safe.

**Disclosure:** All authors have declared no conflicts of interest.

**LONG TERM PERSISTENT ALOPECIA AND SUBOPTIMAL HAIR REGROWTH AFTER ADJUVANT CHEMOTHERAPY FOR BREAST CANCER: ALERT FOR AN EMERGING SIDE EFFECT: FRENCH ALOPERS OBSERVATORY**

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**Background:** Since 2003, through the impetus given by Pr Erick Gamelin and the Regional Health Agency in Western France (Beaupré, Pays de Loire), a network called OMAT (Drugs and Emerging Therapeutics Observatory) has been created, including the Breast Cancer Forum. Anthracyclins and taxanes are the cornerstones of adjuvant chemotherapy for breast cancer. In France, since the PACS 01 publication, FEC 100 followed by docetaxel 100 mg/m^2 has been the standard adjuvant chemotherapy regimen in breast cancer.

**Method:** A single institution retrospective analysis was performed using the Vall d’Hebron University Hospital database to identify EBC pts. Data regarding surgical procedures and tumor clinicopathological characteristics, including margin status, were collected. Margins were classified as PM or CM.

**Results:** Between 2000 to 2009, 85 BC patients, median age 55 years (range 25–94), underwent S2 for PM (82.4%) or CM (17.6%): immediate re-excision (8.8%), late re-excision (30.6%), and mastectomy (61.2%). Median time from S1 to S2 was 3.9 weeks (range 0–32.4). Median time from S1 to the initiation of Tx was 8.9 weeks (range 2–56). 31 pts (37.3%) initiated Tx within 8 weeks (G1) and 54 (63.3%) beyond 8 weeks (G2). With a median follow-up of 4.9 years (0.21–9.8), 12 pts (14.1%) recurred: 3 in G1 and 9 in G2. Median DFS was 8.6 years (95% CI 0.3–9.3). Median OS was not reached as only 4 pts died (all G2). In G1, median DFS was 9.1 years (95% CI 8.2–10 compared with 7.9 years in G2 (95% CI 7.1–8.8), the difference not reaching statistical significance (p=0.355).

No relationship was found between clinico-pathologic characteristics (tumor size, lymph node, histological grade, hormonal receptor, HER2, Ki67, vascular invasion status), type of S2 and timing to Tx.

**Conclusion:** Initiation of systemic treatment is more often delayed in patients with positive/close margins following BCS. Although not statistically significant, most recurrences in our series occurred in group receiving adjuvant chemotherapy beyond 8 weeks of initial surgery. The impact of a second surgery for PM/CN and the consequent delay of adjuvant treatment should be carefully evaluated in clinical practice.

**Disclosure:** All authors have declared no conflicts of interest.

**A MULTICENTER STUDY OF IMAGE-GUIDED RADIOFREQUENCY ABLATION OF SMALL BREAST CARCINOMAS**


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**Background:** Locally ablative therapy of early breast cancer represents the next frontier in the evolution of minimally-invasive breast conservative therapy. We performed this Phase II trial to determine the efficacy and safety of Radiofrequency (RF) ablation of small localized invasive breast carcinomas as a multicenter study in Japan.

**Methods:** Forty patients with core-biopsy proven invasive breast cancer, T1bN0M0 < 2 cm in diameter on ultrasound and MRI were enrolled in this trial. Under ultrasound guidance, the tumor and at least a 5mm margin of surrounding breast tissue were ablated with saline-cooled RF electrode followed by surgical resection. Pathologic and immunohistochemical stains were preformed to assess tumor viability.

**Results:** Thirty-eight patients completed the treatment. The mean tumor size on ultrasound was 1.38 cm. The mean ablation time was 12 minutes using mean power of 80.0 watts. During ablation, the tumor became progressively echogenic that correspond with the region of sever electrocautery injury at pathologic examination. Of the 36 treated patients, HandE and sDNA viability staining was available for 21 patients and in 21 (100%), there was no evidence of viable cancer cells. HandE or sDNA staining were available for another 17 patients. In total, complete thermal injury to the target lesions was recognized in 32 of 38 treated patients (84.2%). No sever adverse effect on the skin and chest wall were noted.

**Conclusion:** RF ablation is a promising minimally invasive treatment of small breast carcinomas, as it can achieve effective cell killing with a low complication rate. We are planning a multicenter observational study for RF ablation of small breast carcinomas.

**Disclosure:** All authors have declared no conflicts of interest.

**TIMING OF SUBSEQUENT SURGERY (S2) FOR POSITIVE MARGINS (PM) AND INITIATION OF ADJUVANT SYSTEMIC TREATMENT (TX) IN EARLY BREAST CANCER (EBC)**

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**Background:** Achieving negative surgical margins during breast-conserving surgery (EBC) is critical to the outcome of EBC patients (pts). On the other hand, the timing of adjuvant systemic treatment (Tx), either chemotherapy or hormonal therapy, is related to EBC prognosis. In this study, we sought to determine if the presence of positive (PM) or close margins ≤ 1 mm (CM) following initial surgery (S1), and the resultant need for S2, would affect the timing of Tx and hence patient outcome.

**Disclosure:** All authors have declared no conflicts of interest.
High-dose chemotherapy (HDC) with autologous stem cell transplantation (ASCT) as adjuvant treatment in high-risk early breast cancer can increase disease-free survival but it failed to improve overall survival in randomized phase III studies. We have performed a retrospective analysis of data available on EMBI registry to analyze the long term outcome of patients (pts) with early stage and operable breast cancer who underwent an adjuvant HDC with ASCT between 1995 and 2005. Objective of the study was to analyze the outcome of the pts > 40 years of age, histological grade, hormonal receptor (HR) and HER-2 expression, menopausal status, number of axillary positive LNs, courses of chemotherapy before HDC, HDC procedure (surgical vs. multiple courses). So far data of 384 pts were collected from the EMBI registry, and additional data were required to the investigators. Histological grade was available in 309 pts, HR status in 382 pts, HER-2 status in 94 pts. Median age was 47 yrs (21-67), 40% of the pts had endocrine sensitive disease and 60% had a high grade disease; 13% of the pts had received reredox adjuvant chemotherapy, and 67% were in premenopausal status. Median number of positive axillary LNs was 12 (3-46). All the pts received standard chemotherapy before HDC: (< 4 courses 81.3 %). A single course of HDC was performed in 84.4% of the pts. At a median follow-up of 120 months (3-182), the DFS and OS at 5 and 10 yrs were 62% and 43%, and 74% and 60% respectively. Transplant-related mortality was 3.3%. OS for pts with grade 1-2 vs. grade 3 disease was 86% vs. 68% and 67% vs. 58% at 5 and 10 yrs respectively (p = 0.002). DFS for pts with < 10 or > 10 positive axillary LNs at 5 and 10 yrs was 76% vs. 57% and 55% vs. 39% respectively. No statistical difference in DFS and OS was observed according to age, HR status, HDC procedure, courses of chemotherapy before HDC. In conclusion, HDC is a safe procedure as a part of a multidisciplinary approach for pts with high-risk primary breast cancer. Optimal role of the this procedure in appropriate and biologically characterized subgroups of pts remains to be evaluated.

Disclosures: All authors have declared no conflicts of interest.

ACCESS OF HIGH-RISK BREAST CANCER PATIENTS TO ADJUVANT CLINICAL RESEARCH PROGRAMS IN FRENCH COMPREHENSIVE CANCER CENTRES: A SURVEY BY THE REMAGUS GROUP

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Objectives: to evaluate what is the “real-life” access of patients with high-risk breast cancer (BC) to ongoing clinical adjuvant research programs in 3 comprehensive cancer centres (CCC).

Patients and methods: We have prospectively evaluated the adjuvantonlineTM-based risks of recurrence and breast-cancer death in all invasive BC patients seen post-operatively by the dedicated multidisciplinary teams of 3 large French CCC during a 1-month period. We evaluated the risks in the absence of treatment as well as the residual risks following optimal treatments planned according to shared guidelines. We noticed whether they were eligible for ongoing adjuvant trials and whether participation was proposed. Major international adjuvant trials were available on-site. High-risk was defined as a calculated residual risk of death > 30% after planned treatments including age, histological grade, hormonal receptor (HR) and HER-2 expression, menopausal status, number of axillary positive LNs, courses of chemotherapy before HDC, HDC procedure (surgical vs. multiple courses). So far data of 384 pts were collected from the EMBI registry, and additional data were required to the investigators. Histological grade was available in 309 pts, HR status in 382 pts, HER-2 status in 94 pts. Median age was 47 yrs (21-67), 40% of the pts had endocrine sensitive disease and 60% had a high grade disease; 13% of the pts had received reredox adjuvant chemotherapy, and 67% were in premenopausal status. Median number of positive axillary LNs was 12 (3-46). All the pts received standard chemotherapy before HDC: (< 4 courses 81.3 %). A single course of HDC was performed in 84.4% of the pts. At a median follow-up of 120 months (3-182), the DFS and OS at 5 and 10 yrs were 62% and 43%, and 74% and 60% respectively. Transplant-related mortality was 3.3%. OS for pts with grade 1-2 vs. grade 3 disease was 86% vs. 68% and 67% vs. 58% at 5 and 10 yrs respectively (p = 0.002). DFS for pts with < 10 or > 10 positive axillary LNs at 5 and 10 yrs was 76% vs. 57% and 55% vs. 39% respectively. No statistical difference in DFS and OS was observed according to age, HR status, HDC procedure, courses of chemotherapy before HDC. In conclusion, HDC is a safe procedure as a part of a multidisciplinary approach for pts with high-risk primary breast cancer. Optimal role of the this procedure in appropriate and biologically characterized subgroups of pts remains to be evaluated.

Disclosures: All authors have declared no conflicts of interest.
proposed adjuvant hormone therapy. Calculated median risks of cancer death and relapse without and after planned treatment were 9% and 26% vs 6% and 14% respectively. Only 34 patients (16%) were considered as patients with a high-risk status. Of them, 8 were Her2+; although these did not have a correct evaluation of risk through adjuvantonline, 7 were eligible for ongoing adjuvant trials; 7 other high-risk cases were triple-negative cases, 6 being eligible for clinical trials; conversely, amongst the 19 high-risk ER+ and/or PgR+Her2- cases left, only 1 patient was eligible in 1 trial.

Conclusion: More than half of high-risk patients bear a luminal B breast cancer profile. While high-risk Her2+ and triple-negative BC patients have a large access to clinical research programs, luminal B patients have currently a very limited access to such adjuvant programs. New strategies are eagerly awaited for this population.

Disclosure: All authors have declared no conflicts of interest.

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**EARLY BREAST CANCER: PROGNOSIS RELATED TO Ki-67 EXPRESSION**

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**Background:** Breast cancer (BC) is the most common tumor in Mexican women between 35 and 50 years old. Ki67 is a nuclear antigen considered as a proliferation marker with potential prognostic significance in BC survival.

**Objective:** To determine a correlation between Ki67 and prognostic factors, recurrence and overall survival in early BC.

**Patients and methods:** From January 2000 to December 2008, pts > 18 yrs old with invasive BC, stages I to IIIB, ductal or lobular, treated with surgery were included. Pts with in situ or inflammatory BC or neoadjuvant chemotherapy were excluded. Pts were divided into four groups according to Ki67 levels: 1) Ki67 < 5%, 2) 6% to 20%, 3) 21% to 50%, and 4) > 51%.

**Results:** 132 pts were analyzed. Groups 1 to 4 were integrated by 23 pts (17.4%), 49 to 50%, and 4) > 51%.

**Conclusion:** More than half of high-risk patients bear a luminal B breast cancer profile. New strategies are eagerly awaited for this population.

Disclosure: All authors have declared no conflicts of interest.

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**ADJUVANT BREAST CANCER CHEMOTHERAPY BASED ON SEQUENTIAL ANTHRACYCLIN AND TAXANE: RETROSPECTIVE ANALYSIS OF HEMATOLOGICAL TOXICITY**

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1Medical Oncology, Instituto Português de Oncologia Dr. Francisco Gentil Porto, E.P.E., Porto/PORTUGAL, 2Medical Oncology Department, Portuguese Institute of Oncology, Porto/PORTUGAL, 3Medical Oncology, Portuguese Institute Instute Porto/PORTUGAL, 4Medical Oncology, I.P.O Porto, Porto/PORTUGAL, 5Medical Oncology, Instituto Português de Oncologia - Porto, Porto/PORTUGAL

**Background:** Anthracyclines and taxanes are the most active cytotoxic drugs for breast cancer (BC) treatment. FEC100-D100 had superior efficacy compared to an anthracycline (A) based regimen, especially in node-positive BC patients. Although myelotoxicity was manageable in different trials, there remain doubts in the clinical application context of A-D sequential therapy.

**Objectives:** Evaluate the hematological toxicity (HT) of FEC-D in the adjuvant setting of BC treatment.

**Methods:** retrospective analysis of clinical records of patients submitted to FEC-D without primary prophylaxis. Relative dose intensity (RDI) was calculated for epirubicin (E) and D. For evaluation of evolution of practice it was made two groups according to the date treatment. Hematological toxicity was defined as grade 3 or 4 according to CTCAE-NCI v4.0. Univariable evaluation and multivariable analysis were made with chi-square and logistic regression analysis respectively.

**Results:** We reviewed 416 consecutive patients, treated between 11/2007 and 06/2009, a total of 2470 treatments. Median age 55.2 years ± 11.8. Because of neuropenia (N) 20

**Abstract:**

<table>
<thead>
<tr>
<th>CMF-like N (%)</th>
<th>Anthracyclines N (%)</th>
<th>Taxanes N (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Classified</td>
<td>9</td>
<td>14.8</td>
<td>26</td>
</tr>
<tr>
<td>ER+ HER2+ Ki67&lt;19</td>
<td>4</td>
<td>37.7</td>
<td>4</td>
</tr>
<tr>
<td>ER+ HER2+ Ki67&gt;19</td>
<td>5</td>
<td>3.7</td>
<td>4</td>
</tr>
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<td>ER+ HER2+ Ki67&lt;20</td>
<td>5</td>
<td>43.2</td>
<td>22</td>
</tr>
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<td>51.9</td>
<td>27</td>
</tr>
<tr>
<td>ER+ HER2- Ki67&lt;20</td>
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<td>10</td>
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<tr>
<td>ER+ HER2- Ki67&gt;20</td>
<td>5</td>
<td>50.0</td>
<td>44</td>
</tr>
</tbody>
</table>

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doi:10.1093/annonc/mdq516 | viii58
Abstract: 239P Table 1

<table>
<thead>
<tr>
<th>pN</th>
<th>N</th>
<th>%CMF-like</th>
<th>N</th>
<th>% Anthracycline</th>
<th>N</th>
<th>% Taxane + anthracycline</th>
<th>N</th>
<th>% Taxane alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>67</td>
<td>13.4%</td>
<td>320</td>
<td>63.7%</td>
<td>100</td>
<td>19.9%</td>
<td>15</td>
<td>3.0%</td>
</tr>
<tr>
<td>pN1</td>
<td>23</td>
<td>5.5%</td>
<td>189</td>
<td>44.8%</td>
<td>190</td>
<td>45.0%</td>
<td>20</td>
<td>4.7%</td>
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<td>pN2</td>
<td>10</td>
<td>12.2%</td>
<td>534</td>
<td>48.8%</td>
<td>420</td>
<td>38.4%</td>
<td>41</td>
<td>3.7%</td>
</tr>
</tbody>
</table>

241P IMPACT OF MAMMAPRINT ON THE ROUTINE TREATMENT DECISION MAKING PROCESS IN AN UNSELECTED EARLY BREAST CANCER PATIENT POPULATION IN BELGIUM

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Background: Multidisciplinary teams nowadays decide on oncological adjuvant treatments by using common clinical and biological criteria. Differences in the quality of IHC analysis and medical board interpretation of prognostic and predictive factors can substantially affect the adjuvant strategy resulting in risks for under- and overtreatment.

The main objective of this study is to compare decisions taken when diagnostic gene expression analysis (70-gene MammaPrint assay) (MP) is added prospectively, to the traditional treatment decision making process in an unselected patient population.

Methods: In 2009, we collected fresh tumour samples during surgery in 162 breast cancer patients. Sufficient RNA for microarray analysis was obtained from 135 patients: MammaPrint Low risk (MP LR) profiles were found in 42%, MammaPrint high risk (MP HR) profiles in 58% of the patients. Following conventional treatment recommendations, 11 of 57 (19%) MP LR patients received chemotherapy and 34 of 78 (44%) MP HR patients received no chemotherapy. The MP HR patients receiving no chemotherapy (CT) and MP LR patients receiving CT were considered unmatched cases and submitted for second opinion to three independent academic teams initially blinded and subsequently unblinded for the MP
Results: According to the initial recommendation (blinded for MP) of these 3 academic teams, 13 of 34 MP HR patients remained without CT and 9 of 11 MP LR patients would still receive chemotherapy. Subsequently, unblinded for the MammaPrint result, these 3 academic teams changed their recommendation in 6 of 13 MP HR patients. Ultimately, from the 78 patients classified as High risk by MammaPrint, 7 remained without chemotherapy treatment recommendation in this multidisciplinary adjuvant treatment planning (9%).

Conclusions: This study demonstrates high variability in the adjuvant strategies between multidisciplinary teams based on traditional patient and tumour related parameters. In our study population, the MammaPrint gene profile would have modified adjuvant treatment recommendation in at least 10% of patients.

Disclosure: All authors have declared no conflicts of interest.

243P THE OUTCOMES OF THE SPECIALIZED GENETIC PROGRAM PROVIDED FOR THE CARRIERS OF THE GENETIC ALTERATIONS PREDISPOSING TO THE BREAST CANCER

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The f-up program for individuals carrying mutations in breast/ovarian cancer predisposing genes has been provided at the specialized unit of the Dept. of Oncol., General Teaching Hospital, Prague, in close collaboration with the Dept. of Med. Genetics and Biochem. and Exp. Oncol. since 1999. The mutation status of the BRCA1 and BRCA2 genes has been analyzed since its beginning, testing of other genes involved in hereditary breast cancer (HBC) development has been introduced later (Table 1). The median f-up of the whole population is 43 months. During this period, 7 malignancies have been found in BRCA1/2 and CHEK2 healthy mutation carriers. One BC has been detected during the initial visit. Median time to the detection of malignancy was 47 months. One BC has been diagnosed in stage 0, 5 in stage 1 and 1 in stage IIb. The first abnormal findings were CA 19-9 elevation in 3 patients, breast MRI in 2 patients, mammography in 1 and breast ultrasound in 1 patient. Six of these BC have been detected during regular f-up visits. One BC occurred as an interval carcinoma. Nine secondary malignancies have been identified among 135 HBC patients carrying mutation in BRCA1/2 (6 BC, 1 ovarian carcinoma, 1 pancreatic cancer and 1 lung carcinoma). 23 risk reducing salpingo-oophorectomies and/or hysterectomies have been performed among 90 healthy BRCA1/2 mutation carriers (26%). In the same cohort, prophylactic mastectomy has been carried out in 4 of 90 women (4.5%). The low proportion of prophylactic surgical procedures is caused by low mean and median age of these women.

Table 1. Basic characteristic of tested population.

<table>
<thead>
<tr>
<th>Analyzed gene</th>
<th>No. tested individuals</th>
<th>No. tested families</th>
<th>No. mut. carriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td>1336</td>
<td>156</td>
<td>190</td>
</tr>
<tr>
<td>BRCA2</td>
<td>1326</td>
<td>48</td>
<td>67</td>
</tr>
<tr>
<td>CHEK2</td>
<td>1336</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>PS1</td>
<td>1211</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>ATM</td>
<td>1211</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Conclusion: Specific preventive program for mutation carriers is an effective option for identification of high-risk BC patients at early and highly curable stages. Acknowledgement: The study was supported by the grant MSM0021620808.

Disclosure: All authors have declared no conflicts of interest.

246P ADJUVANT CHEMOTHERAPY PRESCRIPTION ACCORDING TO MULTIDISCIPLINARY TEAM DECISION OR THE MINDACT PROTOCOL (MICROARRAY IN NODE-NEGATIVE AND 1 TO 3 POSITIVE LYMPH NODE DISEASE MAY AVOID CHEMOTHERAPY) (EORTC100141 BIG 3-04)

C. Mitte, A. Doneux, F. Maioës, V. Samartzi, D. Goddart, Y. Néytscho, B. Pelit, C. Confiéte, M. Beaudulin, R. Gerard
Radiotherapy, Jolimont Hospital, Hainé Saint Paul/BELGIUM

Introduction: The European-based MINDACT trial is a multicentre prospective phase III randomised study. It compares a genomic test (G) (MammaPrint®) developed with microarray technology to traditional clinical-pathological (C) criteria (age, tumor grade, stage, hormone receptor expression) included in a modified version of Adjuvant! Online (AIO) for assessing the risk of recurrence in women with lymph node negative or 1-3 node positive breast cancer. Patients assessed as “High Risk” by both MammaPrint® and AIO are advised to have CT whereas for those assessed “Low risk” by both methods no chemotherapy is recommended. Discordant cases are randomised to treatment decision based on G or C criteria. We compared the prescription of CT defined by the protocol to the one decided in the multidisciplinary tumour board as traditionally done.

Materials and methods: Among the 35 patients enrolled between May 2008 and January 2010, 16 patients were classified as low risk (CL-GL) by both methods, 4 patients were classified as high risk (CH-GH) by both methods and 15 patients were in the discordant group.

Results: The 16 CL-GL patients did not receive CT in accordance with the protocol. Eight of these patients would have been proposed CT by the tumour board. The 4 CH-GH patients were proposed CT in accordance with the protocol and would also have been recommended CT by the tumour board. For the 2 patients with a CL-GH randomised to no CT, the decision was also identical between the protocol and the tumour board.

Among the 13 patients with CH-GH, 12 would have received CT according to the tumour board while following the protocol randomisation only seven received CT. Overall, from the 35 patients included, 15 (43%) avoided CT due to the MINDACT protocol.

Conclusions: Since breast cancers with similar clinical characteristics can have strongly different outcomes, even if treated similarly, the current decision-making for adjuvant CT needs to be improved. If the added value of the molecular profile is validated, a personalisation of the treatment strategy could be considered for each patient.

Disclosure: All authors have declared no conflicts of interest.

247P IMPACT OF DIFFERENT PROGNOSTIC FACTORS ON THE DEVELOPMENT OF BRAIN METASTASIS IN ADJUVANT BREAST CANCER PATIENTS

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Background and aim: The brain is increasingly being recognized as a sanctuary site for metastatic tumor cells in high risk breast cancer patients. Symptomatic brain metastasis develop in 10%-20% of patients with metastatic breast cancer, most often following disease progression at other sites, carrying a poor 1- and 2-year survival rates of only 20% and <2%, respectively.

Patients and methods: We retrospectively analyzed breast cancer patients eligible for adjuvant systemic treatment who presented to us in the period from 2000 till 2006. Relationship between BFS and different factors was done.

Results: There were total 36 courses of chemotherapy for the 15 patients included in our study. The means of CEC, V-CECs and CEP were all significantly decreased in the 1st week of chemotherapy compared to those in the Day 1 of treatment, the differences were -2.05/L, 95% CI (-3.90, -0.21); -1.57/L, 95% CI (-3.00, 0.14); and -0.41/L, 95% CI (-0.60, -0.20) respectively. After 1st week of chemotherapy, the means of CEC, V-CEC, CEP came back to a similar level compared to Day 1 of treatment. The differences were 0.07/L, 95% CI (-1.71, 1.85); 1.11/L, 95% CI (-1.49, 1.70); and -0.34/L, 95% CI (-0.54, 0.16) respectively. There is a trend towards increase in total number of CEP after cycles of chemotherapy. The other factors including existence of tumor, status of operation, drug used, and use of GCSF, were not statistically significantly affected these results.

Conclusions: Although the CECs and CEPs decrease in one week after chemotherapy, the number recovered soon, and with a trend towards increase in CEP number after several cycles of chemotherapy. The possible impact of this phenomenon on tumor re-grow warrant further studies.

Disclosure: All authors have declared no conflicts of interest.
Results: Our study included 1752 patients of which 75 developed brain metastasis. The 3-year BDFS was 84.5% for ER+ve, 86.4% for PR+ve, 84.2% for Her-2/neu+ve patients compared to 93.5% for ER+ve (p<0.001), 93.7% for PR+ve (0.006) and 92.5% for Her-2/neu–ve (0.002) patients respectively. Patients with grade III tumors had a lower 5-year BDFS of 41.2% compared to 93.1% for those with grade I-II disease (p<0.001). Positive lymph nodes had a marginal significance of a lower BDFS as well (96.2% vs. 94.9%; p=0.042). There was no significant difference seen according to age, pathological type or menopausal status. In a multivariate analysis model, histological grade and negative hormonal receptor status were the most significant. Her-2/neu score was missing in a quite a large number of patients which did not allow us to draw solid conclusions regarding its predictive value. By comparing BDFS among different subgroups of Breast cancer namely Hormone Receptor positive (HR+), Her2 positive (Her2+) and Triple negative (TN), no statistical significant difference was found with median BDFS of 35.7, 26.3, 26.9 months respectively (p=0.487).

Conclusions: Patients with poorly differentiated tumors appear to have a higher probability of developing brain metastases as well as those with negative hormonal status. We could not draw solid conclusions regarding the predictive value of Her-2/neu gene. These patients could be good candidates for trials investigating the role of any prophylactic intervention to decrease their risk to develop brain metastases.

Disclosure: All authors have declared no conflicts of interest.

244P ARE BREAST CANCER (BC) PROGNOSTIC FACTORS DIFFERENT IN YOUNG PATIENTS?

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Background: BC in young patients has worse prognosis than older women, but a clear identification of prognostic factors in this population is still fuzzy. The aim of this study was to find independent predictors of disease free survival (DFS) and overall survival (OS) in patients aged < 40 years.

Materials and methods: Data of 219 women (mean age 35±4) were retrospectively analyzed (period: 1996-2008). Clinico-pathological and follow-up data were derived from medical records. Kaplan Meier method and Cox regression model were used to obtain survival curves and independent prognostic factors, respectively.

Results: Table 1 reports the histological features of study population. Follow-up data were available (mean 75±31 months) for 214 patients (98%). Of these, 10% developed local relapse, 25% distant relapse, 3% contra-lateral BC and 3% second tumor. DFS and OS were significant different for stage (p<0.001 for both), pN (p<0.001 and p<0.01, respectively), LHRh-analogues therapy (p<0.005 and p<0.05, respectively) and amenorrhea (p<0.05 for both). At univariate analysis, stage (HR 1.82, p<0.001), pN (HR 1.99, p<0.005), LHRh-analogues therapy (HR 0.49, p<0.005) and amenorrhea (HR 0.58, p<0.05) were significant predictors of DFS, while stage (HR 2.25, p<0.01), pN (HR 2.03, p<0.05), MIB-1 (HR 2.3, p<0.05), G (HR 2.4, p<0.01), LHRh-analogues therapy (HR 0.42, p<0.05) and amenorrhea (HR 0.42, p<0.05) of OS. At multivariate analysis, only stage maintained a significant relevance for DFS (HR 2.08, p<0.001) and OS (HR 2.05, p<0.05).

Conclusions: In young BC patients, prognostic relevance appears to be symbolized by different factors than in older women; in particular, hormonal changes induced by therapy seem to influence prominently outcomes. Our results indicated that there are chemo-resistant populations with hormone receptor positive BC.

Disclosure: All authors have declared no conflicts of interest.

244P PREDICTIVE FACTORS FOR COMPLETE PATHOLOGICAL RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER. RESULTS FROM A SINGLE INSTITUTION

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Introduction: Pathological complete response (pCR) has been identified as the most important prognostic factor for survival in the neoadjuvant setting for breast cancer. The aim of our study was to assess both clinical and molecular factors with prognostic importance in a series of patients with stage IIA-IIIB breast cancer treated with neoadjuvant chemotherapy (CT).

Material and methods: We performed a retrospective analysis of predictive factors for pCR in stage IIA-IIIB breast cancer treated with neoadjuvant CT in Hospital Clinico de Valencia from 1993 to 2001. Potential molecular and clinical prognostic factors were recorded from medical history. Univariate and multivariate analysis was performed in order to assess prognostic value of each variable.
Annals of Oncology

Results: Median age of the 170 patients included, was 56 years (43.8-64.3), 57.1% were premenopausal and 42.9% were postmenopausal. Estrogen receptors in our series were positive in 64.2%, progesterone receptors were positive in 44.7%. Grade was I in 11.2%, II in 55.9% and III 32.9%. HER2 was positive in 21%. Clinical stage was IIA 36.6%, IIB 23.3%, IIA 20.3% and IIB 19.8%. Surgery of the primary tumor was conservative in 39.4% and mastectomy in 60.6%. Patients received a median of 4 cycles (3-8) of neoadjuvant CT, 70.3% with anthracyclines and 29.7% with anthracyclines associated with taxanes. pCR obtained was 14% in schedules with anthracyclines and 23% in CT containing both anthracyclines and taxanes. In the univariate analysis, patients obtaining pCR presented significantly an increased rate of grade 3 tumors and negative estrogen and progesterone receptors. Patients with pCR completed an increased number of cycles of CT and surgery underwent was more frequently conservative. In the multivariant analysis molecular prognostic factors maintaining significance were grade and estrogen receptors.

Conclusions: Negative estrogen receptors, and grade 3 are both predictive factors useful for decision in the neoadjuvant setting. Tumors with these features are strongly associated with an increased probability of obtaining pCR in this setting.

Disclosure: All authors have declared no conflicts of interest.

THE 70-GENE EXPRESSION PROFILE FOR BREAST CANCER PATIENTS IN ITALIAN HOSPITALS

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1) The St Gallen (C.D. Spielberger) to evaluate State and Trait Anxiety. 2) A specifically designed questionnaire (26 items) to evaluate informative, emotional and interactive dimensions of the counselling interview and genetic testing indication.

Results: The survey was conducted in 100 consecutive subjects: 59% affected patients and 41% probands. The proportion of patients <50 years in 53% of subjects. The majority of the subjects were females and 66% had at least a high school degree. The vast majority of the subjects (84%) reported to be satisfied with the consultation, the proportion being slightly higher in patients (49%) as compared to probands (39%). Sixty-nine percent of the responders seemed to understand the implications and consequences of genetic testing with no apparent difference between the 2 subgroups. As regards the psychological impact, 78% of the population reported the same level of concern and fear as compared to pre-counseling.

Conclusions and future perspectives: Overall, the preliminary results showed a high degree of satisfaction in terms of well-being during the consultation, clarity and understanding of the information given. The degree of anxiety before and immediately after counselling, as specifically investigated by the STAI instrument, is being currently analysed. Next steps include a detailed qualitative analysis of weaknesses and limits of the questionnaire (i.e. type and formulation of some questions) in order to develop an improved tool to be shared with different cancer genetic services in Northern Italy.

Disclosure: All authors have declared no conflicts of interest.

EVALUATION OF COMPLETENESS AND QUALITY OF THE INFORMATION PROCESS DURING GENETIC COUNSELLING FOR CANCER PREDISPOSITION. PRELIMINARY RESULTS OF THE GENETIC COUNSELLING SERVICE (GCS) OF SOUTHERN SWITZERLAND

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Introduction: Phase I studies showed the way information is provided can impact patients’ comprehension of risk, their concerns and anxiety, the last two dimensions being generally overestimated by physicians. Informative and relational dimensions of cancer predisposition assessment can affect individuals’ quality of life and negatively impact their psychological condition.

Subjects and methods: A pilot prospective survey assessed satisfaction and distress associated with genetic counselling in patients and probands of the GCS of Southern Switzerland. Subjects were given: 1) The STAI (C.D. Spielberger) to evaluate State and Trait Anxiety. 2) A specifically designed questionnaire (26 items) to evaluate informative, emotional and interactive dimensions of the counselling interview and genetic testing indication.

Results: The survey was conducted in 100 consecutive subjects: 59% affected patients and 41% probands. The proportion of patients <50 years in 53% of subjects. The majority of the subjects were females and 66% had at least a high school degree. The vast majority of the subjects (84%) reported to be satisfied with the consultation, the proportion being slightly higher in patients (49%) as compared to probands (39%). Sixty-nine percent of the responders seemed to understand the implications and consequences of genetic testing with no apparent difference between the 2 subgroups. As regards the psychological impact, 78% of the population reported the same level of concern and fear as compared to pre-counseling.

Conclusions and future perspectives: Overall, the preliminary results showed a high degree of satisfaction in terms of well-being during the consultation, clarity and understanding of the information given. The degree of anxiety before and immediately after counselling, as specifically investigated by the STAI instrument, is being currently analysed. Next steps include a detailed qualitative analysis of weaknesses and limits of the questionnaire (i.e. type and formulation of some questions) in order to develop an improved tool to be shared with different cancer genetic services in Northern Italy.

Disclosure: All authors have declared no conflicts of interest.

BREASTFEEDING IN BREAST CANCER SURVIVORS: PATTERN, BEHAVIOUR AND EFFECT ON BREAST CANCER OUTCOME

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Introduction: We have recently presented a meta-analysis confirming the safety of pregnancy in breast cancer (BC) survivors [Azim HA Jr et al; EBCC 2010]. However, very little is known regarding the safety and feasibility of breastfeeding in these women

Methods: We searched the database of the European Institute of Oncology from 1988-2006 for women ≤ 40 years at BC diagnosis. We constructed a questionnaire and performed a survey among patients who had a completed pregnancy following BC therapy to examine their lactation behaviours and its effect on BC outcome.

Results: 32 women were identified, 20 were reachable and accepted to take the survey. 15 women were previously subjected to breast conservative surgery (BCS) while the rest were subjected to mastectomy. Only 15 (50%) women initiated breastfeeding. The main reasons for not initiating breastfeeding were “uncertainty regarding maternal safety” and “a priori unfeasibility” expressed either by the obstetrician or by the medical oncologist. In those who breastfed their babies, 4 stopped within 1 month and 6 had long-term success with a median period of 11 months (7-17 m). The latter were all previously subjected to BCS and received lactation counselling at delivery. Out of 15 women who underwent BCS and radiotherapy, 14 reported hypoplasia of the irradiated breast during pregnancy. 7/15 attempted to breastfeed from the affected breast but milk production was significantly reduced with difficulty in latching. Only 2 women were able to breastfeed from both breasts but only for 2 weeks. At a median of 48 months following delivery, all 20 women were alive with Zelapes; 1 in each group (i.e. lactating and non-lactating)

Conclusions: Breastfeeding from the affected breast is challenging but exclusive lactation from the contralateral breast is feasible. Previous mastectomy was associated with short lasting (<1 month) breastfeeding, even if all women who had a previous BCS used 1 breast for lactation. This emphasises the importance of body image in the
Materials and methods: The study group consisted of 34 premenopausal women with breast cancer. The diagnosis was histopathologically proven and hormone receptors were positive.

Objective: In this study, we intended to investigate osteoporosis progression in the early stages after ovarian ablation in premenopausal women with breast cancer whose hormone receptors were positive.

Results: The measurements of patients and control groups in baseline showed no significant statistical difference. Patients observed over 2 years (18/34) had no significant statistical difference in calcium, phosphate, ionized calcium, ALP, FSH, LH, estradiol, urine deoxyprydioline, osteocalcin, and PTH were obtained. Lumbar spine and femur bone mineral density was measured.

Discussion: All authors have declared no conflicts of interest.
FEATURES OF RECURRENCE OF TRIPLE NEGATIVE (TN) NON-METASTATIC BREAST CANCER (NMBC) PATIENTS: A SINGLE INSTITUTION STUDY

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Background: TN breast cancer (BC) are the most agressive type of BC, and we do not have a target therapy against this type. Our goal is to determine the rate of recurrence, the affected organs and the DFS in these patients.

Materials and methods: We reviewed 1042 charts of all diagnosed BC patients from January/2000 to December/2005 and choose 215 who were TN-NMBC. The data was analyzed by analytic and descriptive statistics in SPSS v. 17.0

Results: The rate of TN-NMBC were 20.6%(215) of them 18.6%(40) patients had recurrences with an average age of 52.5(13-93) years. The median DFS were 27 months with a median follow-up of 64 months. The Stage I, II and III were 7.5%(3); 32.5%(13) and 69%(24) respectively for patients with recurrence. The most frequent involved organs with recurrence were visceral (lung and liver) 43.7%(15), bone 23%(10), skin 20%(8), CNS 12.5%(5) and contralateral breast 5%(2). Additionally we found five patients with history of familial BC, and four of them were stage II with negative lymph node at diagnosis.

Conclusion: TN-NMBC are 20.6% of all BC, the majority of them were stage III (60%), the median DFS for patients with recurrence were 27 months, and the most frequent sites involved were visceral (37.5%) and bone (25%). It is very interesting pay attention even in early stages to patients with history of familial BC for risk of recurrence, BRCA positive!

Disclosure: All authors have declared no conflicts of interest.

RETROSPECTIVE ANALYSIS OF TRIPLE-NEGATIVE BREAST CANCER IN ONE HUNGARIAN CENTER

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Genetic investigations have unveiled the great diversity of breast cancers even in the triple-negative subtype. 10% of the generally high-risk triple-negative breast cancers (TNBC) are of low metastatic potential and have favorable prognosis even without adjuvant systemic therapy. There is a great need to investigate disease group to reach better prognostic accuracy and treatment efficacy. There are publications dealing with the characteristics of TNBC, but only rare data derives from Middle East Europe.

Material: The database of National Institute of Oncology in Hungary was searched for early TNBC operated from January 2005 to October 2008. Clinical and pathological characteristics were investigated in connection with survival data. Patient charts were excluded where other malignancy were known in the previous 10 years or where no data could be collected about perioperative treatment and survival.

Results: Charts of 234 female patients were eligible. Mean age at clinical presentation was 56.3 years (25-86 y). 31 patients were younger than 40. The tumours were typically invasive ductal carcinoma (80%) with high histological grade (93.6%). According to staging: St I/Ii/Iii 31%(46.7%)22%. Lymph node metastasis was present in 41%. Pathologic report described necrosis (71%), lymphocyte infiltration (80%), extensive vascular invasion (14%) and p53 (53%) in many cases. However, 89% of patients were given perioperative chemotherapy with a median of 42.6 months follow-up, 65 relapses and 46 deaths occurred. Stage, lymph node status, type of adjuvant chemotherapy and vascular invasion showed significant impact on survival.

Conclusion: Genetic testing is an attractive method for predicting prognosis and chemo-resistance, high costs hinders its widespread use. Classical pathologic assessment still has additional possibilities to better characterize breast tumors certainly with rigorous standardization.

Disclosure: All authors have declared no conflicts of interest.

CLINICAL RESPONSE OF TRIPLE NEGATIVE BREAST CANCER TO TAXANES

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Background: Most of triple-negative breast cancer (TNBC) have close association with the BRCA1 gene dysfunction. It has been demonstrated that BRCA1 genotype affects sensitivity of breast cancer to chemotherapeutic agents. DNA-damaging agents such as platinum are promising in the treatment of TNBCs harboring BRCA1 dysfunction.

Objective: The aim of this study is to analyze the clinical response of TNBC patients to the neoadjuvant chemotherapy with taxanes.

Patients and methods: Between 2003 and 2010 at our institutes, patients were retrospectively selected for this study according to the following criteria: (1) Female breast cancer patients who received 4 cycles of doxorubicin (60 mg/m^2) or epirubicine (90 mg/m^2) and cyclophosphamide (600 mg/m^2) every 3 weeks followed by 12 cycles of weekly paclitaxel (80 mg/m^2) or 4 cycles of triweekly docetaxel (75 mg/m^2) as a neoadjuvant setting. (2) Patients who were evaluated by the imaging studies as CT or MRI following in the three points: 1) before treatment, 2) after anthraclyines and 3) after taxanes. A total of 71 patients fulfilled the eligibility criteria for this study. We compared the clinical responses of TNBCs to taxanes with that of non-TNBCs.

Result: There were 24 TNBCs (33%). The median age of TNBCs was 52 years (31-68 years). Eight and 16 patients were clinical stage II and III respectively. Twenty-three patients received weekly paclitaxel, and one patient received triweekly docetaxel. Overall clinical responses of AC/(EC) followed by taxanes in TNBCs were 91% (CR; 5; PR; 17). Primary tumor progression was seen in 4 patients (16.6%) while receiving taxanes. One of 4 patients experienced progressive disease (PD) by the RECIST criteria. Four patients with tumor progression were associated with young age or having family history or great response to anthracyline. No tumor progression while receiving taxanes occurred in the patients with non-TNBCs.

Conclusion: These data suspect that TNBCs, especially associated to BRCA dysfuction, may be less sensitive to taxanes in clinical settings.

FAKTORS INFLUENCING THE TIME OF SENTINEL NODE VISUALIZATION IN BREAST CANCER PATIENTS USING INTRADERMAL INJECTION OF THE RADIOTRACER

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Background: The objective of our study was to determine the important factors which have influence on the time of sentinel node visualization using intradermal injection of Tc-99m-antimony sulfide colloid.

Method: 250 consecutive patients with the diagnosis of early stage breast cancer were evaluated. Anterior and lateral views were acquired in various intervals after intradermal injection of the tracer till 180 minutes or visualization of the sentinel node. The effect of several variables on the time of sentinel node visualization was evaluated by univariate and multivariate analyses.

Results: The time of sentinel node visualization was significantly correlated with age, BMI, and interval between biopsy and sentinel node mapping. Standardized beta values for these variables were 0.1, 0.3, -0.55 respectively.

Conclusions: Older age and higher BMI can result in slow sentinel node visualization. Longer interval between biopsy and sentinel node mapping can be associated with rapid sentinel node detection.

Disclosure: All authors have declared no conflicts of interest.

SENTINEL LUMP NODE MAPPING IN EXCISIONAL BIOPSY

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Background: To date, the number of excisional biopsies continues to increase. This is due to the desire of patients for aesthetic and psychological reasons. In these cases, sentinel lymph node mapping is still not commonly used. This study evaluated the sentinel lymph node mapping technique in excisional biopsy.

Method: In this study, 126 consecutive patients were enrolled. All patients underwent an excisional biopsy. Sentinel lymph node mapping using blue dye was used in all patients. In total, 116 patients were able to be evaluated for sentinel node mapping. Mean age in this group was 49 years (range: 25-75 years).

Results: The node was detected in 74 patients (64.5%) and was negative in 36 patients (31.5%). The mean time of sentinel node visualization was 120 minutes (range: 30-180 minutes). The detection rate of sentinel node was significantly and positively correlated with the number of levels excised.

Conclusion: Sentinel lymph node mapping in excisional biopsy is a feasible and cost-effective technique. Further research is needed to evaluate the long-term outcomes and complications of this technique.

Disclosure: All authors have declared no conflicts of interest.
Background: The idea of using neoadjuvant chemotherapy in patients with operable breast cancer is supported by experimental and clinical observations as well as theoretical hypotheses on tumor cell growth and dissemination. Several recently reported trials of neoadjuvant therapy incorporating newer agents such as taxanes in some patients have shown further increases in pathological complete response (pCR) rates. We conducted a single center phase II study to evaluate the anti-tumour activity of docetaxel in combination with doxorubicin for neoadjuvant therapy of patients with operable breast cancer.

Patients and methods: Thirty-eight women were treated with intravenous doxorubicin 50 mg/m^2 over 15 min followed by a 1-h infusion of docetaxel 75 mg/m^2 every 3 weeks for six cycles. Dexamethasone and anti emetic drugs as premedication was allowed. Granulocyte colony-stimulating factor was not given as primary prophylaxis. The primary end point was the pathological response rate and its corollation with the improved outcomes.

Results: In our interim analysis, the overall pathological response rate was 13%. There were 9 complete and 24 partial clinical responses for an overall response rate of 89% (95% confidence interval (CI) 75% to 95%) in the evaluable population (n = 37). Disease-free and overall survival rates were 85% (95% CI 71% to 94%) and 96% (95% CI 85% to 99%), respectively, after a median follow-up of 36.6 months. Grade 3/4 neutropenia was observed in 46% of patients and 13% reported grade 4 febrile neutropenia.

Conclusions: Docetaxel and doxorubicin is an effective and well-tolerated neoadjuvant chemotherapy in operable breast cancer patients.

Disclosure: All authors have declared no conflicts of interest.

261 PHASE II STUDY OF DOCETAXEL AND DOXORUBICIN COMBINATION AS NEOADJUVANT CHEMOTHERAPY IN OPERABLE BREAST CANCER PATIENTS

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262 PREGNANCY AND BREAST CANCER

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Background: Choosing proper tactics for the treatment of pregnancy-associated breast cancer (PABC) remains very complicated.

Methods: We have performed an analysis of treatment outcomes of 87 patients with PABC, who underwent treatment in N.N. Petrov Research Institute of Oncology in 1992-2009. In 29 patients tumor was detected during pregnancy, in 58 – during lactation (first months after childbirth). In 57 (62.3%) patients early BC (T1-2N0-M0) was detected, in 22 patients – locally-advanced BC (T3-4N1-2M0), 25 patients had metastatic BC. The control group consisted of 242 patients with BC not associated with pregnancy, who had received treatment in the same time frame. It included 128 patients with early BC, 56 patients with locally advanced BC and 58 patients with metastatic disease. Patients with locally advanced BC received FAC (70%) or TAC (30%) neoadjuvant chemotherapy. All patients with early BC and about 80% of patients with locally-advanced BC (after neoadjuvant chemotherapy) underwent surgery: 43 of 59 had mastectomy and 10 patients had breast-conserving surgery in PABC group. Patients with metastatic disease in both groups received CMF, FAC or taxane-based chemotherapy.

Results: 7 year mean follow-up showed no significant difference in survival of patients who underwent surgery either for early or for locally advanced BC either associated with pregnancy or not (75.3% and 77%, respectively). Moreover, no difference in overall survival between patients with PABC and non-associated with pregnancy BC was found (68% vs 62% P=0.58). There was no difference in overall survival between groups of patients with metastatic PABC and non-associated with pregnancy BC (14.6 and 15.6 months, respectively).

Conclusion: No significant difference in survival between patients with PABC and non-associated with pregnancy BC was found. Though there is an obvious connection of prognosis and survival with clinical stage of disease and detection of locally advanced form.

Disclosure: All authors have declared no conflicts of interest.

263 MALE BREAST CANCER

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Background: Male breast cancer is rare; it constitutes 0.2-1.3% of all malignant tumours in men and 1% of all breast cancers.

Patients and methods: The goal of this retrospective study is to analyse the epidemiologic, clinic, therapeutic and effective profiles of this disease in 122 cases collected at the National Institute of Oncology in Rabat, Morocco, between the years 1997 and 2007.

Results: The median age was 60 years (27-90). The average consultation’s delay was 14 months. The main clinical complaint was a mass beneath the areola in 98% of the cases, associated with ulceration in 39% of the cases. For that, the disease was diagnosed at an advanced stage. Infiltrating ductal carcinoma was the most frequent pathologic type (96%, 60 cases). Lymph node involvement was found in 93% of cases. The oestrogen and progesterone receptors were positive in 92%. Management consisted especially of radical mastectomy, followed by adjuvant radiotherapy and hormonal therapy or without chemotherapy. It was possible to follow 100 of the patients. The median of follow-up was 40 months. The five-year disease free survival and OS rates were 66% and 82% respectively. The evolution has been characterized by local recurrence, after a median delay of 12 months, in 2 cases. Metastasis occurred, after a median delay of 16 months, in 27 cases (53% of all patients). The site of metastasis was the bone in 10 cases, lung in 8 cases, liver in 8 case and skin in one case. There were 2 cases of death. Progression was observed in one case.

Conclusion: Male breast cancer is a rare disease (about 1% of breast cancer) with a poor prognosis (32% 10 years disease free survival). An early diagnosis and better knowledge of the disease would certainly lead to improvement of prognosis.

Disclosure: All authors have declared no conflicts of interest.

264 AN EXPLORATORY STUDY TO CONFIRM OR REFUTE THE NOVEL HYPOTHESIS THAT IATROGENIC HYPERCORTISOLISM CAUSES OSTEOPOROSIS IN BREAST CANCER SURVIVORS ON AROMATASE INHIBITORS

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Background: To determine if aromatase inhibitors (AIs) cause accumulation of upstream adrenal biosynthetic intermediates with diversion of hormones down the 1717 (OH) progesterone, 11-deoxycortisol and a 24 hr urinary free cortisol were measured. Also the bone formation upstream adrenal biosynthetic intermediates with diversion of hormones down the 17

Methods: Breast cancer patients that had been treated with AIs for 12-48 months were identified. Serum androsteondione, DHEAS, 17 (OH) progesterone, 11-deoxycortisol and 24 hr urinary free cortisol were measured. Also the bone formation
OUTCOME IN YOUNG WOMEN WITH BREAST CANCER: MOROCCAN EXPERIENCE

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Background: Breast cancer is uncommon in young women and correlate with poor prognosis. The aim of this study was to determine demographic and molecular characteristics, outcome and prognostic factors in young women with breast cancer.
Methods: Four hundred and ninety women aged less than 35 years were diagnosed with breast cancer at the national institute of oncology between 2003 and 2007. Demographic, molecular and treatment characteristics were taken from patient record. The relation between pathologic and clinico-therapeutic characteristics with event-free survival (EFS) and overall survival (OS) was assessed.
Results: Median age was 32 years. Fifty three patients (13%) had metastatic disease at diagnosis. Three hundred and 56 patients (87%) had localized disease. Twenty-eight patients (9.9%) had a family history of breast cancer. BCMA mutation was diagnosed in only one patient and was positive. Fifty eight % of the patients had estrogen receptors (ER) positive. ERBB-2 gene amplification was detected in 57 patients and was positive in 28. Three hundred and 47 patients received surgery for localized disease. Seventy six patients (21.3%) received neoadjuvant chemotherapy from which 2 patients had pathologic complete response. The median follow-up was 32.2 months. Patients with stage I, II, III and IV disease had 100%, 89.3%, 74.7%, and 57.8% survival after 3 years respectively. This difference was statistically significant (p<0.001). In patients with localized disease. In multivariate analysis, we showed that ER negative status was the only prognostic factor significantly influencing the OS (HR = 2.43, 95% CI = 1.25-4.66, p=0.009). Also, ER status and stage III disease were the only factors associated with poorer EFS (HR = 1.73, 95% CI = 1.05 - 2.86, p=0.03 and HR = 5.35, 95% CI = 1.60 - 17.84, p=0.01 respectively).
Conclusions: Breast cancer is a rare condition in women aged ≤35 years. It had aggressive clinical and biological behaviors. From our retrospective investigation we confirmed that factors influencing survival and event free survival in univariate and multivariate analysis were the stage of disease and the ER status. Research and clinical trials were needed in young women with breast cancer to improve their outcome.
Disclosure: All authors have declared no conflicts of interest.

PRE-METASTATIC NICHE IDENTIFICATION IN NODE-NEGATIVE BREAST CANCER TO ASSESS METASTASIS RISK. PATHOLOGICAL AND CLINICAL IMPLICATIONS

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Approximately 20% of patients (pts) with infiltrative node negative breast cancer (BC) at the time of surgery will relapse within 10 years. Bone marrow-derived hematopoietic progenitor cells (HPCs) seem to participate in early spread of cancer cells by forming a peculiar and highly organized mini-environment, called pre-metastatic niche (PMN). Identifying such HPCs in the PMNs is emerging as a key step in assessing risk of metastasis. We immunohistochemically analyzed 626 nodes (603 pN0 and 23 pN1a) obtained from 511 pts undergone surgery for ductal invasive BC, in the period 1998-2007, in order to verify if HPCs may represent the first step of the metastatic spread and correlate immunohistochemical data and clinic-pathological characteristics. Formalin-fixed paraffin-embedded 4-μm-thick serial sections were treated with the following polyclonal antisera: VEGF-R1, CD 133, CD 117, CD 34; CD 34 and CD 117 appeared as the most useful HPCs markers, whereas Rh1- and CD 133 exhibited a variable rate of immunostained elements. After a median follow-up of 62.6 months (6–136), 29 pts are still alive; 23 disease-free and 6 with metastases. 18 pts dead: 16 for BC and 4 for other causes. 4 pts are lost to follow-up. The main metastatic sites were bone, lung and liver. A significant relationship (p<0.001) was found between immunohistochemical detection of HPCs and development of metastasis, high Ki67 values as well mortality for BC. Our data show that immunomorphologic aspect of node microenvironment could provide a powerful tool for identification of patients at high risk of metastases, in order to optimize BC therapeutic strategies and reduce morbidity and mortality.

MEDIAN AGE 62.05 years (41-85)
RECEPTOR
ER+ PgR+ 39%; ER− PgR− 35.6%; ER+ PgR− 16.4%; ER− PgR+ 12.0%
STATUS
HER2 negative 33%; unknown 57%; (2+) 6%; (3+) 4%
STAGE
pT1 53 %; pT2 37.2%; pT3 7.8%; pT4 2%

Disclosure: All authors have declared no conflicts of interest.

BREAST INVASIVE LOBULAR CARCINOMA. IS IT WORTH DOING ANY COMPLEMENTARY STUDY?

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Aims: The purpose of this study was to determine the status of different histologic markers in invasive lobular carcinoma (ILC), to categorize this histologic type with the novel molecular classification and to check the matching cytokeratin. Methods: 39 patients with invasive lobular carcinoma who underwent surgery at the Rio Currion General Hospital between 1997 and 2005 had tissue available for analysis (age range, 37-88 years; mean, 65 years). Estrogen and progesterone receptors (ER, PR), E-cadherin, Her2/new, Ki-67, CKs 8/18 and CKs 5/6 were evaluated by immunohistochemical analysis (IHC). Her2/new was also evaluated by SISH (Silver In Situ Hybridization), together with the chromosome 17 centromere.
Results: All cases were E-cadherin negative. All the ILCs were ER positive. EP were positive in 12 cases (32%). CKs 8/18 were positive in all cases and CK 5/6 were entirely negative; 24 cases (61.5%) were Her2/new negative. Among Her2/new positive cases (17.9%) 1+ and 8 (20.5%) were 2++; we found no case considered as 3+.

Inhibitors were noted in 23% of premp and 25% of postmp pts. Recurrence was seen in 7 premp N0A without DFS 68.7 % and in 14 postmp pts (17.3%) with mDFS 30.7 m. In the group with recurrence on /after TMX therapy were inactivated pms of CYP2D6 (IM+PM) detected in 42% of premp pts and in 50 % of postmp. Comd with CYP2D6 inhibitors we noted in 14% of premp pts and in 28% postmp pts with disease recurrence.
Conclusion: Our preliminary results do not clearly support the hypothesis that the polymorphisms of CYP2D6, MDR-1 and the comedication with CYP2D6 inhibitors can influence the efficacy of TMX therapy.
Disclosure: All authors have declared no conflicts of interest.
SISH analysis, no case showed amplification of Her2/neu. With this technique one case showed a chromosome 17 polisomy and 4 showed monosomy (10.8%).

Conclusions: All the ILCs were considered as luminal type and, as the ductal counterpart, they expressed low molecular weight cytokeratins (CKs 8/18). To being set in this category could explain the good prognosis, the good response to endocrine therapy and the low pathologic response after non-adsorbing chemotherapy that characterizes this tumor. Interestingly, we describe for the first time a chromosome 17 monosomy in ILC, and may be related to a inactivation of tumour-suppressor genes. As Her2/neu is the biological target for trastuzumab therapy and no overexpression has been described, it seems reasonable that ILCs patients cannot benefit from this costly treatment. As Her2/neu is the biological target for trastuzumab therapy and no overexpression has been described, it seems reasonable that ILCs patients cannot benefit from this costly treatment and this would avoid the associated toxicity. Moreover, if ILCs are correctly diagnosed, it may be unnecessary to determine ILC and Her2/neu status.

Disclosure: All authors have declared no conflicts of interest.

NEW PREOPERATIVE CHEMOTHERAPY WITH LYPOSOMAL ANTHRACYLINE, CIPISTATIN AND METRONOMIC CAPECITABINE FOR OPERABLE AND LOCALLY ADVANCED BREAST CANCER: DATA OF EFFICACY AND SAFETY

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Background: The main goal of preoperative chemotherapy is the achievement of pathological complete remission (pCR). We report the data of activity and safety of the anthracycline-containing regimen MCV with the introduction of oral fluoropyrimidine capecitabine as preoperative chemotherapy for large operable and locally advanced breast cancer.

Methods: Patients with operable breast cancer (T2-3) or locally advanced breast cancer (T4, N2-N3) were treated with non-pegylated liposomal doxorubicin (Myocet 50 mg/m2 day 1), ciplatin 60 mg/m2 day 1 and metronomic capecitabine 1500mg daily continuously (MCX) for six courses followed by radical surgery and radiotherapy. In patients whose tumours were endocrine-responsive concurrent endocrine therapies (letrozole if postmenopausal or triptorelin if premenopausal) were given preoperatively. All patients had a core biopsy and a basal surgical evaluation to define type of surgery and pathological response after neoadjuvant chemotherapy. 16 patients were evaluable for clinical response, thirteen patients are evaluable also for pathological response. There were 4 pCR (31.3%), 12 partial remissions (PR) (91.6%, 75%) and 4 complete remissions (CR) (4/16, 25%). Six patients out of 13 received breast conserving surgery. The worst toxicity was non febrile grade 4 neutropenia in 2 pts (15%), grade 3 anemia in 1 pt (8%), nausea/emesis grade 2 in 10 pts (50%) and alopecia in 6 (33%).

Results: Twenty patients were enrolled. Median age was 51 years (range 29-71), premenopausal 44%. At the core biopsy: ER and/or PR > 1% in 60%, Ki-67 expression 20% in 67%, Her2/neu negative in all patients. Clinical stage at diagnosis was II B in 20%, IIIA in 30%, IIIB in 30% and IIIC in 15%. Sixteen patients are evaluable for clinical response, thirteen patients are evaluable also for pathological response. There were 4 pCR (31.3%), 12 partial remissions (PR) (91.6%, 75%) and 4 complete remissions (CR) (4/16, 25%). Six patients out of 13 received breast conserving surgery. The worst toxicity was non febrile grade 4 neutropenia in 2 pts (15%), grade 3 anemia in 1 pt (8%), nausea/emesis grade 2 in 10 pts (50%) and alopecia in 6 (33%).

Conclusions: This combination is effective as preoperative treatment. The combination of metronomic capecitabine in an anthracycline-containing regimen is promising in terms of clinical activity and safety.

Disclosure: All authors have declared no conflicts of interest.

LONG TERM SURVIVAL OF EARLY AND LOWLY ADVANCED BREAST CANCER PATIENTS TREATED OUTSIDE OF CLINICAL TRIALS

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Background: Data on outcome of patients treated in community settings is scarce and may be different from clinical trials.

Methods: Retrospective review of all patients treated in a general oncology academic private practice between 1997-2007. Patients with non-metastatic breast cancer at presentation and have available follow-up were included. Patients were staged or restaged according to AJCC 7th edition. DFS was calculated from time of diagnosis till time of distant recurrence. Overall survival was calculated from time of diagnosis till time of distant recurrence.
time of last follow-up or death. Study was approved by IRB of the American University of Beirut. Data was entered and analyzed using SPSS. Survival was calculated and estimated according to Kaplan Meier method.

Results: Total number of patients with primary non-metastatic breast cancer was 383. There were 14 cases of DCIS and/or LCIS. Analysis was carried out on remaining 369 patients with invasive breast cancer with complete follow-up. 25% of pts had stage I, 45% had stage II and 30% had stage III (Locally Advanced Breast Cancer: LABC) Stages I: Total number was 93 pts. Median age at diagnosis was 49 yrs (Range 23-77 yrs). 12% had missing receptor status. 76% had positive hormonal receptors. Overall Survival (OS) at 5 years was 98%, at OS at 10 years 92%. Stage II: Total number was 167 pts. Median age at diagnosis was 48 yrs (Range 31-85 yrs). 14% had missing receptor status. 67% had positive hormone receptors. OS at 5 yrs was 90% and OS at 10 yrs was 78%. Stage III (LABC): Total number was 109 pts. Median age at diagnosis was 48 yrs (Range: 21-78 y). 17% had missing receptor status. 65% had positive hormone receptors. OS at 5 yrs was 68% and OS at 10 yrs was 34%. Partial mastectomy was mostly performed in earlier stages and mastectomy for more advanced cases. Pre-operative therapy, adjuvant chemotherapy, hormonal therapy and radiation therapy were conformal with standard current guidelines. Adjuvant trastuzumab was used starting June 2005. Patients were followed closely every three months and compliance with therapy was excellent.

Conclusions: Application of stringent modern multimodality therapy learned from clinical trials for breast cancer results in excellent 5 and 10-year survival rates in stages I and II in clinical practice. OS for stage III drops to 68% at 5 years and 34% at 10 years indicating continued need for early detection to improve outcome and survival of newly diagnosed patients with breast cancer.

Disclosure: All authors have declared no conflicts of interest.

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BREAST CANCER IN THE KINGDOM OF SAUDI ARABIA (KSA). A REVIEW OF ALL MALE BREAST CANCER (MBC) CASES FROM THE SAUDI CANCER REGISTRY (SCR) FROM 1994-2004


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Introduction: KSA is divided into 13 administrative regions (AR) and the first case registered in the SCR was in January 1994. SCR through 5 regional offices collects all cancer cases. Cancer site and histology are coded using the International classification of Disease for Oncology (ICD 0-3) and the SEER staging system as the main reference for the data collected. The aims were to identify trends of (MBC) incidence, differences in age, stage and regional distribution over years in KSA.

Methods: We analyzed SCR data. All statistical analysis was done using the statistical software package SAS version 9.2. Descriptive statistics were reported for all variables. All categorical variables were summarized in frequencies and percentages. Similarities and differences with female counterparts were analyzed.

Results: 6655 cases of breast cancer (BC) were found. 156 were (MBC) and included. MBC represented 2.3% of all BC. The median age was 58 (25-100) years with interesting regional differences. The incidence was low 0.1 to 0.5/100000 but did not reveal a steady increase over years. Important regional differences noted with majority of cases reported from 3 regions namely Makkah, Riyadh and eastern province with a steady increase over years in these three regions. 3.2% had pure in Situ disease (DCIS). More than 71% of cases were invasive ductal cancer (IDC), followed by 20% Carcinoma/Adenocarcinomas. Medullary carcinomas 6.4%. Lobular carcinomas (LC) 1.92 %. and 1.2% Paget’s disease. Staging revealed regional with or without nodal involvement 36%, 18.8 % have metastatic disease and about 24% were localized and in 18 % stage unknown.

Conclusions: MBC is an uncommon form of BC our incidence in higher than the reported in literature of less than 1%. There are regional differences in incidence and rate of metastatic disease remained high. MBC has important differences and similarities to female breast cancer. The difference include , lower incidence, 10 years higher median age , higher rates of DCIS and lower rates of LC and steady incidence contrary to increasing in females. Similarities include IDC being most common histology and similar staging. Multicenter collaboration is needed to optimize management of this uncommon cancer.

Disclosure: All authors have declared no conflicts of interest.