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 based on country practices. All data were collected and analyzed at the Central Data Center in Leiden. In total, 99% of patients were E+ or E+/PgR+, 50% were node-negative, 44% underwent mastectomy, 68% received radiotherapy, and 36% received chemotherapy. Thirteen patients withdrew consent.

Results: Based on an intention-to-treat analysis, among 9,767 patients 420 DR occurred in patients randomized to T—E and 408 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 0.93; 95% confidence interval 0.81–1.07; p-value 0.31). Table: Sites of 1st reported DR

<table>
<thead>
<tr>
<th></th>
<th>T—E arm (4868)</th>
<th>E arm (4898)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N 5y cum inc</td>
<td>N 5y cum inc</td>
</tr>
<tr>
<td>Bone only (1)</td>
<td>115 2.5%</td>
<td>2.0 - 3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>116 2.4%</td>
</tr>
<tr>
<td></td>
<td>2.0 - 2.9</td>
<td></td>
</tr>
<tr>
<td>Visceral only (2)</td>
<td>122 2.5%</td>
<td>2.1 - 3.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>99 2.1%</td>
</tr>
<tr>
<td></td>
<td>1.7 - 2.6</td>
<td></td>
</tr>
<tr>
<td>Bone+Visceral</td>
<td>90 1.9%</td>
<td>1.5 - 2.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>92 2.0%</td>
</tr>
<tr>
<td></td>
<td>1.6 - 2.5</td>
<td></td>
</tr>
<tr>
<td>Other/unknown (3)</td>
<td>93 2.0%</td>
<td>1.7 - 2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>93 1.9%</td>
</tr>
<tr>
<td></td>
<td>1.5 - 2.3</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>420 8.9%</td>
<td>7.3 - 10.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 8.8%</td>
</tr>
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<td></td>
<td></td>
<td>8.4 - 10.3</td>
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</tbody>
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(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 similar between both arms (Rea, SABCS 2009). The present analysis explores the sites of first reported distant recurrences (DR).

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 Pfizer, AstraZeneca and Novartis. He has also disclosed that he is a consultant for Pfizer AstraZeneca and Novartis. He has also 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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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.

216PD ABCSG-24: EFFICACY OF ANTHRACYCLINE-AND TAXANE-BASED NEOADJUVANT THERAPY + CAPECITABINE (G) 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 Suppl 2009;7:3 (Abst 4BA)). Here we assess whether the addition of G produces a pCR benefit in patients with TNBC.

Methods: Patients with biopsy proven operable breast cancer, except T4d, with TNBC were randomly assigned to either ED + G (n = 324) or ED (n = 338) arm. 

Results: 103 pts are eligible for safety and efficacy assessment (255 ED; 253 G). 

Conclusions: Addition of G 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] 3.29, 95% CI 3.22-8.68; p = 0.0011), this was true irrespective of the regimen used. The highest pCR rates were attained with the addition of C to ED in patients with TNBC (47.5%), representing a 16% increase in pCR rate vs the ED group (31.2%), but this was not significant. There was no interaction between C therapy and TNBC in terms of pCR (p = 0.675).

**Regimen** | **pCR, n (%)** | **p value**
--- | --- | ---
EC/G | TNBC (n=122) | non-TNBC (n=348) | OR (95% CI) |
--- | --- | --- | --- |
EDC/ED | 48 (39.3) | 38 (10.9) | 5.29 (3.22, 8.68) | <0.0001 |
EDC | 29 (47.5) | 23 (13.2) | 5.95 (3.05, 11.59) | <0.0001 |
ED | 19 (31.2) | 15 (8.6) | 4.80 (2.25, 10.23) | <0.0001 |

Disclosure: M. Gnant: Research support and consultancy fees from AstraZeneca, Novartis, and Pfizer as well as lecture fees and honoraria for participating in advisory boards from AstraZeneca and Amgen. A. Lang: Dr. Lang received an unrestricted research grant from Jansen Cilag. C. Singer: Amgen research grant received, 10000 Euro / 3 years. M. Gnant, On Behalf of The Austrian Breast and Colorectal Cancer Study Group (ABCSG). Research support from and serving as a consultant for AstraZeneca, Novartis, Roche, Schering, Amgen, and Pfizer: B. Minertische: Lecture fees and honoraria for participation in advisory boards - GlaxosmithKline, Pfizer, Sanofi, Cephalon. G. Luschin-Ebengrueh: Lecture fees - AstraZeneca, Novartis. S. Poestlberger: Lecture fees - AstraZeneca, Novartis and Roche. G. G. Steger: Dr. Steger received lecture fees from AstraZeneca and Novartis. R. Ja克斯: Consultancy and honoraria for participation in advisory boards - AstraZeneca, Roche, Sanofi-Aventis; Lecture fees - AstraZeneca, Roche, Sanofi-Aventis. H. Stoeger: Dr. Eidtmann received honoraria for participation in advisory boards and lecture fees from AstraZeneca and Novartis. R. Greil: Consultancy and honoraria for participation in advisory boards - AstraZeneca. All other authors have declared no conflicts of interest.

217PD ADJUVANT ENDOCRINE THERAPY, ALONE OR IN COMBINATION WITH ZOLEDRONIC ACID (ZOL), IN PREMENOPAUSAL PATIENTS (PTS) WITH ENDOCRINE- RESPONSIVE EARLY BREAST CANCER (EBC): SUBGROUP ANALYSES OF ABCSG-12 

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Background: Initial 48-month results of the ABCSG-12 trial, which examined the efficacy of ovarian suppression using goserelin in combination with tamoxifen (TAM) or anastrozole (ANA) a ZOL in premenopausal pts with EBC, showed that adding ZOL significantly reduced the risk of disease-free survival (DFS) events by 36% (P = 0.01). However, no differences were seen between TAM and ANA. Longer follow-up results are presented here.

Methods: Premenopausal pts with EBC (N = 1803) were randomized to goserelin (3.6mg q28d) and TAM (20mg/d) or ANA (1mg/d) ± ZOL (4mg q28d). Endpoints included DFS and overall survival (OS); both were analyzed using log-rank test and Cox models.

Results: After a median follow-up of 62 months, 186 DFS events and 66 deaths were reported. Overall, ZOL reduced the risk of DFS events by 32% (HR = 0.68 [95% CI = 0.51, 0.91]; P = 0.008) vs no ZOL. The risk reduction by ZOL was nearly identical in the TAM and ANA arms (HR = 0.67 [0.44, 1.03]; P = 0.065 for TAM, HR = 0.68 [0.45, 1.02]; P = 0.059 for ANA). Similarly, ZOL had a nearly identical risk reduction for node-negative (N–) and node-positive (N+) pts (HR = 0.66 [0.43, 1.03]; P = 0.063 for N–, HR = 0.67 [0.45, 0.91]; P = 0.043 for N+). Overall, ZOL produced a 35% trend toward reduced risk of death (HR = 0.65 [0.40, 1.06]; P = 0.087). The OS benefit was more pronounced in the N+ subgroup (HR = 0.61; P = 0.05). There was no difference in DFS between pts who received TAM alone vs ANA alone (HR = 1.11 [0.84, 1.50]; P = 0.44); however, ANA pts did worse with respect to OS (HR = 1.74 [1.05, 2.87]; P = 0.03) vs TAM, likely because of differences in post-relapse treatment. Treatments were generally well tolerated, with no cases of renal failure or osteonecrosis of the jaw reported.

Conclusions: Addition of ZOL (4mg q28d) in the ABCSG-12 trial consistently improves disease outcomes in the TAM and ANA strata, and in N– and N+ pts, although there was no difference in DFS between TAM and ANA. ANA pts had inferior OS vs TAM, likely due to fewer treatment options after relapse. Based on these results and the known anticancer activity of adjuvant ZOL, adding ZOL to endocrine therapy could benefit premenopausal pts with EBC.

Disclosure: M. Gnant: Research support and consultancy fees from AstraZeneca, Novartis, and Pfizer as well as lecture fees and honoraria for participating in advisory boards from AstraZeneca and Amgen. R. Jakesz: Consultancy and honoraria for participation in advisory boards - AstraZeneca, Roche, Sanofi-Aventis; Lecture fees - AstraZeneca, Roche, Sanofi-Aventis. H. Eidtmann: Dr. Eidtmann received honoraria for participation in advisory boards and lecture fees from AstraZeneca and Novartis. R. Greil: Consultancy and honoraria for participation in advisory boards - AstraZeneca. All other authors have declared no conflicts of interest.

**Regimen** | **DFS (n=122)** | **OS (n=122)** |
--- | --- | ---
EDC/ED | 48 (39.3) | 38 (10.9) |
EDC | 29 (47.5) | 23 (13.2) |
ED | 19 (31.2) | 15 (8.6) |

The Development of a Formulation of Trastuzumab for Subcutaneous Administration

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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 18–52 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 (rHuPH20) 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 aims of the Phase Ib study were to select the dose of a new subcutaneous trastuzumab formulation with HRP4204 giving 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 6 mg/kg IV maintenance dose. The 8 mg/kg dose of the subcutaneous trastuzumab resulted in a C_{max}, 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, diarrhoea, lethargy and nausea. Injection site reactions included discolouration, 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 favourable. These results support further testing of subcutaneous trastuzumab.

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

## Methods:

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

Results: The median SD percent change of Ki-67 after 3 weeks was -9.3%±3.2% in the lapatinib arm and +15.1%±30.9% 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 cytotoxic PTEN overexpressing tumors (p=0.057). In post-treatment surgical specimens, the median (range) Ki-67 LI was 15% (5-35) on lapatinib versus 20% (9-66) on placebo in ductal intraductal neoplasia (p=0.06), and 1% (1-15) 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).

Conclusion: 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. Marré-Brunenghi: GSK employer. All other authors have declared no conflicts of interest.
Purpose: The Oncotype DX 21-gene Recurrence Score (RS) assay quantifies the risk of distant recurrence of breast cancer in patients with lymph node-negative, estrogen receptor-positive breast cancer and predicts magnitude of chemotherapy benefit. U.S. studies have shown an impact in clinical decision making. Whether RS might affect medical oncologist adjuvant treatment recommendations in a GEICAM setting.

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 recommendation are available from 71 cases. RS <18 (25 (33.2%) with intermediate RS), RS 18-30 (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 hormone 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% 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%.

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

Acknowledgments: RTCCG support, IGSI, Spain.

Disclosure: E. Alba, R. Colomer, J. Palacios, I. Fauil and M.J. Corominas: Participated in advisory board meetings of Genomic Health Inc and Pales; M. Ruiz-Norrego and J.A. Garcia Saenz: Participated in advisory board meetings of Palex; E. Alba and M. Martin: Participated in advisory boards of Genomic Health Inc; A. Luch: Participated in advisory board meetings of Genomic Health Inc.

ECONOMIC IMPACT OF ONCOTYPE DX ASSAY IN AXILLARY NODE NEGATIVE BREAST CANCER, (AXN-BC) WITH POSITIVE HORMONE RECEPTOR (REC)+AND NORMAL HER-2 (HER-2) by E. Wilson1, D. McDonnell2, G. Gullo3, J. Healy4, G. Carolli5, G. Schroéfeld6, J. Barlow7, J.P. Crown8

Background: Approximately 70% of patients (pts) with AxN-BC are cured by loco-regional therapy. For pts with rec+ disease, adjuvant endocrine therapy (ETs) reduces the relapse risk (RR) by approximately 1/3. Adjuvant chemotherapy (CTx) reduces RR a further 1/3, and is widely used. Thus 90% of pts may receive unnecessary or futile CTx. The validated Oncotype DX assay (OTDx) 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 Trials (EOCG) While widely used in the USA, there is limited European experience with OTDx. We studied the potential economic impact of OTDx based on a large single institution European experience.

Methods: The tumours of 140 pts with AxN-BC were studied using OTDx on TailorRx which uses modified risk group classification. Pts with RS <11 received ETs only, RS 11-25 ETs +/- CTx by randomization, and RS>25 received ETs + CTx. DS decision was to preserve and presence of lymphovascular invasion was also made. The cost of OTDx testing the entire cohort and administering CTx (4 x
doctaxel 75 and cyclophosphamide 600), to those in different RS group, was compared to giving Ctxs to pts based on classic pathology. The unit cost of OTDx was Euro 2.911 and the drug costs of TC4 + GCSF-C=436,246 Results: Using standard criteria, a total of 108/140 pts would have received Ctxs, at a cost of €1.432M. OTDx cost for 140 pts €407K. OTDx.

Results: LR 24, IR 89, HR 27. The CRx cost for 27 hi-risk was €358K, and for 116 high +intermediate risk was €1.538. The CRx cost for pts with RS<18 is approximately €358K.

Conclusions: On a strict drug-cost versus OTDx cost comparison (which does not include institutional overhead and staff costs and thus understates CRx cost), the OTDx assay will result in savings for European health systems if RS<18 is used as criteria for LR, or if CRx is reserved for TailorRx-defined HR. The final economic impact of the OTDxs will depend on the results of the TailorRx trial.

Disclosure: All authors have declared no conflicts of interest.

LETRAZOLE OR ANASTROZOLE FOR THE TREATMENT OF HORMONE POSITIVE BREAST CANCER: A CLINICAL COMPARISON USING INDIRECT STATISTICAL TECHNIQUES by S. Kaura1, G. Dramanisitis2

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Background: Letrozole (LET) and anastrozole (ANA) are more effective than tamoxifen (TAM) in preventing disease recurrence in postmenopausal women with early stage breast cancer. Recent data from BIG1-98 study also suggests that LET may improve overall survival (Regan SABCS, 2009), a finding that has not been demonstrated with ANA. Notwithstanding, there are no data available from head-to-head randomized phase III trials comparing the clinical and non-inferiority between LET and ANA. In the absence of such data, an indirect statistical comparison between LET and ANA was performed. Such an analysis is feasible in this case because Tam was the common comparator in both trials and patients had similar baseline characteristics.

Methods: Data in terms of early distant recurrences, disease free survival (DFS) and overall survival (OS) were extracted from the BIG 1-98 and ATAC trials. After a median follow up of 74 months, the hazard ratio (HR) for OS based on an inverse probability censoring weighted (IPCW) analysis for LET was 0.83 (95% CI 0.71 - 0.97, p = 0.005). From ATAC after a follow up of 68 months, the HR was 0.97 (95% CI: 0.83 to 1.12, p = 0.70). An indirect statistical comparison between LET and ANA was then performed on early distant recurrences, DFS and OS using the method of Bucher et al. (1997), which maintains in part the benefits of randomization on the effect size.

Results: There was little difference between the two drugs with respect to DFS (HR=0.98, 95%CI:0.83 to 1.15). However, the analysis did identify a substantial risk reduction for early distant recurrences between 2 to 2.5 years with LET (HR=0.75, 95%CI: 0.52 to 1.07) over ANA. This translated to a trend for improved OS with LET (HR=0.86, 95% CI: 0.70 to 1.05).

Conclusion: Keeping in mind the caveats associated with cross trial comparisons, this indirect statistical comparison suggests that LET may be more effective than ANA in reducing early distant recurrences and mortality at 5 years. It is possible that the reduction in early distant metastases with LET is responsible for the later improvement in OS. Ongoing trials (FACE, MA27) comparing the aromatase inhibitors should help us confirm the potential survival benefit with LET.

Disclosure: S. Kaura: Mr. Kaura is an employee of Novartis. G. Dramanisitis: Mr. Dramanisitis has received consultancy fees and research funding from Novartis in relation to the research.
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 tamofoxifen 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 tamofoxifen 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 both timepoints). In the tamofoxifen group, a mean increase 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 tamofoxifen (P<0.05 at both timepoints). Bone turnover markers decreased from baseline with tamofoxifen 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 changes appeared to stabilise after initial treatment.

Disclosure: All authors have declared no conflicts of interest.

Methods: 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 HER- 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, 2,203 (95%) were HER2+; 79% (n=1,720) had HER2+ and 63% (n=203) had inconclusive HER2 status. Ninety-two percent of actively treated HER2+ patients 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 received trastuzumab vs. <0.01%). No age differences were observed between patients receiving trastuzumab and those not receiving trastuzumab.

Results: Elevation of serum HER2 ECD levels appeared to be a risk factor for the failure of breast cancer treatment. In the 564 patients treated with adjuvant chemotherapy or tamoxifen for breast cancer in the Adjuvant Group Trial, elevation of serum HER2 ECD levels was negatively associated with overall survival (p = 0.008). Multivariate analysis confirmed that elevated serum HER2 ECD levels were associated with disease progression in patients with metastatic breast cancer, with a trend towards significance (p = 0.08). In the 117 patients treated with tamoxifen and tamoxifen plus exemestane for hormone receptor-positive breast cancer in the NSABP B-18 study, serum HER2 ECD levels were positively associated with disease-free survival (HR = 2.29 (confidence interval: 1.38 – 3.81) for patients with elevated serum HER2 ECD levels vs. patients with normal serum HER2 ECD levels).

Results: In the group of patients with stage II breast cancer treated with adjuvant chemotherapy, the most frequently used regimen was the anthracycline-containing combination chemotherapy regimen of doxorubicin and cyclophosphamide (28.9%), followed by cyclophosphamide, doxorubicin and methotrexate (17.4%) and cyclophosphamide and methotrexate (10.6%). The most frequently used adjuvant hormone therapy was tamoxifen (62.3%). In patients with stage III breast cancer treated with adjuvant chemotherapy, the most frequently used regimen was the anthracycline-containing combination chemotherapy regimen of epirubicin and cyclophosphamide (25.1%), followed by cyclophosphamide, epirubicin, and fluorouracil (19.5%) and cyclophosphamide and fluorouracil (15.5%). The most frequently used adjuvant hormone therapy was tamoxifen (84.4%).

Results: In the group of patients treated with postoperative chemotherapy, the most frequently used regimen was the anthracycline-containing combination chemotherapy regimen of doxorubicin and cyclophosphamide (28.9%), followed by cyclophosphamide, doxorubicin and methotrexate (17.4%) and cyclophosphamide and methotrexate (10.6%). The most frequently used adjuvant hormone therapy was tamoxifen (62.3%). In patients treated with postoperative hormone therapy, the most frequently used adjuvant hormone therapy was tamoxifen (84.4%).

Results: In the group of patients treated with adjuvant or neo-adjuvant chemotherapy, the most chemotherapeutic agents used were anthracyclines, taxanes and cyclophosphamide. Anthracyclines were used in 77% of patients, taxanes in 72% and cyclophosphamide in 51% of patients.
Disclosure: D. Dondi: Employed at sanofi-aventis as Medical Advisor Oncology. All other authors have declared no conflicts of interest.

**236P**  ANTHRACYCLINE AND CONCURRENT RADIOTHERAPY SIGNIFICANTLY REDUCED BREAST CANCER RELAPSE RATE

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**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 (group B).

**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) was at 5 years 98.7% in group A and 95.3% 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 1.016; log-rank P = .057). The median overall survival (OS) was 83.2% and 79.2% in the anthracycline and CMF groups respectively (HR = 0.708; 95% CI 0.455 to 1.128; log-rank P = .057). The 5 years overall survival (OS) was 83.2% 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 = .007) and OS (HR = 0.63; 95% CI 0.401 to 0.991; P = .046). LRFs, 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). LRFs and EFS were significantly higher in the anthracycline group in the breast conservative therapy subgroup (P = .049 and P = .04, respectively).

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

**Conclusion:** We conclude that the treatment based on anthracycline and concurrent radiotherapy reduced breast cancer relapse rate including locoregional relapses and significantly improved LRFs, 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.

**236P**  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 (BCS) 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.

**Methods:** 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 clinical-pathological characteristics, including margin status, were collected. Margins were classified as PM or CM.

**Results:** Between 2000 to 2009, 85 BC pts, median age 55 years (range 25–94), underwent S2 for PM (84.2%) or CM (17.6%): immediate re-excision (8.2%), 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 2–56.7). 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 (0.21–9.18), 12 pts (14%) recurred: 3 in G1 and 9 in G2. Median DFS was 8.6 years (95% CI 6.9–9.2). 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, histologic 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 patients receiving adjuvant chemotherapy beyond 8 weeks of initial surgery. The impact of a second surgery for PM/CM and the consequent delay of adjuvant treatment should be carefully evaluated in clinical practice.

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

**236P**  A MULTICENTER STUDY OF IMAGE-GUIDED RADIOTHERAPY ABERRATION 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, T2-T3a,b 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 immunohistochcmical 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 38 treated patients, HandE and NADPH viability staining was available for 21 patients and in 21 (100%), there was no evidence of viable cancer cells. HandE and or ssDNA 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 severe 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.

**236P**  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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1Medical Oncology, Clinique Víctor Hugo, Le Mans/FRANCE; 2CRCLC Eugène Marquis, Rennes/FRANCE; 3CH Le Mans, Le Mans/FRANCE; 4CRCLC Paul Papin, Angers/FRANCE; 5Centre Emile le Douté, Saint-Nazaire/FRANCE; 6CHoS Lorient, Lorient/FRANCE; 7CHU Morvan Brest, Brest/FRANCE; 8Centre Cathérine de Sierno, Narbon/France; 9CH Quimper, Quimper/FRANCE; 10OMT, Angers/FRANCE

**Background:** Since 2003, through the impetus given by Pr Erik Gamelin and the Regional Health Agency in Western France (Bretagne, Pays de Loire), a network called OMT (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/m² has been the standard adjuvant chemotherapy regimen in breast cancer.

**Disclosure:** All authors have declared no conflicts of interest.
Methods: At the beginning of 2008, the first cases of persistent alopecia or suboptimal hair regrowth after adjuvant chemotherapy have been reported to the Breast Cancer Forum. Consequently, OMIT quickly drew up a case report form and mailed it to every oncologist in Western France to collect data. Afterwards, an adapted quality of life questionnaire was sent to the patients of the ALOPERS observatory.

Results: From May 2008 to May 2010, 108 cases of persistent alopecia or suboptimal hair regrowth after adjuvant chemotherapy from 15 different institutions were declared to OMIT: median age: 59 years (35-78). 96% received a docetaxel-based treatment as adjuvant chemotherapy. More often with docetaxel 100 mg/m² and 77% as hormonal therapy. 50 patients have answered to the questionnaire: 10 are still using a wig. Some patients have suboptimal regrowth of eyelash (55%), eyebrow (75%), pubic hair (33%), 38% and 45% of patients complained of a moderate to severe alteration of the quality of their family and social lives. First dermatological results will be presented.

Conclusions: For the first time in France, Western OMIT offers us data about persistent alopecia or suboptimal hair regrowth after adjuvant chemotherapy: this is an important side effect and it must be considered by oncologists as optimal information to curable patients to discuss about alternative regimens, as weekly paclitaxel. OMIT is currently working on prevention and reduction of these alopecias through ALOPREV trial (cooling scalp system used during docetaxel).

Disclosure: All authors have declared no conflicts of interest.

Background: A study conducted in Italy (NORA, Annals of Oncology 26; 17: 1386-1392) investigated the factors that affected therapeutic decisions in patients who had undergone surgery for early breast cancer (EBC) between 2009 and 2003. Five years later, a new retrospective observational study (NEMESI) was conducted to compare and how attitudes to the adjuvant treatment of EBC patients have changed in Italy.

Results: A total of 3515 patients were enrolled in NORA and 1984 patients in NEMESI, respectively. 68.3% and 57.8% of patients (p=0.0001) received chemotherapy (+/– endocrine therapy), which is in accordance with an earlier diagnosis. The use of CMF-like regimens decreased from 37.1% in NORA to 9.1% in NEMESI (p=0.00001). An anthracycline-containing regimens decreased (from 52.1% to 48.8%; p=0.0001). In particular, “three-drug” regimens decreased (38.9% vs 25.5%), whereas there was a highly significant increase in the use of regimens containing anthracyclines and taxanes, combined in sequence (38.4% vs 0.9%, p<0.00001). The use of taxanes alone remained low (3.5% vs 3.7%, ns). The overall use of anthracyclines and taxanes increased from 53.0% to 87.1% and from 4.3% to 42.5%, respectively; both differences are highly significant (p=0.00001).

Conclusions: Attitudes to adjuvant chemotherapy regimens for EBC have changed over recent years. In fact, CMF regimens are now rarely used, whereas the administration of taxanes, used combined or in sequence with anthracyclines, has greatly increased. This positive trend reflects the fact that once chemotherapy is deemed necessary, the best available regimen should be used, which is represented by third-generation anthra/taxanes. Sponsored by Sanofi-Aventis – Italy.

Disclosures: S. Supelak. I am employed at sanofi-aventis until end of June 2010, as Medical Advisor Oncology. M. Venturini. Membership of the advisory board of this study. All other authors have declared no conflicts of interest.
**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, 32 > 18 years old with invasive BC, stages I to III, 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 30%, 4) 31% to 55%.

**Results:** 132 pts were analyzed. Groups 1 to 4 were divided by 23 (17.4%), 49 (37.1%), 39 (29.3%) y 21 (15.9%); median age 48, 48, 51, 48 yrs (P > 0.05), respectively. Conservative surgery in 56.4%, 50.7%, 25.6% y 42.9%, respectively. In each group, adjuvant chemotherapy was indicated in 82.6%, 83.9%, 90% y 94.7%, respectively. Radiation 47.8%, 36.7%, 43.5% and 42.8%; hormone therapy 63.2%, 71.4%, 59.1% and 90.9%.

**Conclusion:** Higher cellular proliferation through Ki67 is related to poor prognosis factors and higher frequency of recurrence of the disease and lower time of survival in early BC.Ki67/MIB1 plays a key role in the decision to prescribe adjuvant CT in endocrine-sensitive BC. Type of CT selected is not influenced by biological subtype. Ki67/MIB1 is crucial for the prescription of adjuvant CT: 37.5% and 62.3% of pts received adjuvant CT with Ki67/MIB1<20% and with Ki67/MIB1>19%, respectively. Amongst 106/1195 pts receiving adjuvant CT, type of treatment was not influenced by biological classifications.
Background: NEMESI examined the clinical practice in the Italian Oncology Institutions on adjuvant treatment in EBC. 

Methods: This retrospective observational study describes adjuvant treatment in EBC in Italy, involving, between January 1 and June 30, 2008, at least 1,500 cases, 30 consecutive in each center and representative of the Italian situation, in terms of geographical distribution and type of institution, as evidenced from the census reported on the white Book of the Italian Association of Medical Oncology (AIOM). 

Inclusion criteria: age ≥ 18 years, histological diagnosis of early stage operated breast cancer (stage I-II TNM AJCC version VI), ≥1 cycle of adjuvant chemotherapy (CT) and/or hormone therapy. 

Results: A total of 1,848 were included. Tumor characteristics: pT1; 67.0% (22.3%: pT1mic + pT1a + pT1b); pT0: 61.0%; pT1: 29.1%; pT2: 6.3%; pT3: 3.6%; ER pos (20%): 81.2%; ER neg (0-9%): 18.6%; median Ki67: 17%; HER2 pos: 16% (10%): 81.2%; ER neg (0-9%): 18.6%; median Ki67: 17%; HER2 pos: 16%. 

Adjuvant treatment without CT was administered in 799 patients (42.2%), while the remaining 1,049 (57.8%) received systemic CT. Administration of CT is influenced by pN: 43.5% of pts with pN0 received CT, 76.6% of pts with pN1; 89.1% of pts with pN2; 94.2% of pts with pN3. In the pN0 group administration of CT is influenced by pT: 30.6% of pts with pT0 1.0-1.0 cm received CT; 64.4% of pts with pT1 1.1-2.0 cm; 71.6% of pts with pT2 2.1-3.0 cm. Type of CT used is influenced by recurrence risk. The use of Anthracycline and Taxanes increases with risk: pN1 45.0%, pN2-pN3 >70%. 

Conclusions: Italian Oncology Centers frequently use adjuvant CT in EBC. Choice of adjuvant CT is well influenced by prognostic factors (pT and pN). There is still widespread use of first-generation CT drugs, independent from disease severity. In particular for pN0-pN1 class there is an underuse of taxane-based regimens, which is more common in pN2 class. Administration of CT is influenced by pT and pN. Administration of CT is influenced by recurrence risk. The use of Anthracycline and Taxanes increases with risk: pN1 45.0%, pN2-pN3 >70%. 

Disclosure: M. Venturini: Membership of the advisory board of this study. S. Rossi: Employed by sanofi-aventis as Medical Advisor in Oncology, Medical Department. All other authors have declared no conflicts of interest.

Abstract: 239P Table 1

<table>
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<th>N</th>
<th>%CMF-like</th>
<th>N</th>
<th>% Anthracyline</th>
<th>N</th>
<th>% Taxane + anthracyline</th>
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<th>% Taxane alone</th>
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</table>
Annals of Oncology

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.

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 follow-up of the whole population was 41 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 28 months. One BC has been diagnosed in stage 0, 5 in stage I 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 internal 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. 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 ages of these women.

Table 1. Basic characteristic of tested population.

<table>
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<th>Analyzed gene</th>
<th>No. tested individuals</th>
<th>No. tested families</th>
<th>No. mut. carriers</th>
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<td>190</td>
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<tr>
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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.

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) (EORTC10041 BIG 3-04)


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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® (AO) 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 AO 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-GL randomised to no CT, the decision was also identical between the protocol and the tumour board.

Among the 13 patients with CH-GL, 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.

DYNAMICS OF CIRCULATING ENDOTHELIAL CELLS AND ENDOTHELIAL PROGENITOR CELLS IN BREAST CANCER PATIENTS RECEIVING CYTOTOXIC CHEMOTHERAPY

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Background: Anti-angiogenic therapy has become an important field in cancer treatment. Few studies have described circulating endothelial cells (CECs) and circulating endothelial progenitor cells (CEPs) values change after cycles of chemotherapy. However, there is no study to describe the CEC and CEP dynamic change during each consecutive cycle of chemotherapy in human, of which may give us a way to evaluate the timing of adding anti-angiogenic agents.

Materials and methods: We collected blood samples from breast cancer patients who received systemic chemotherapy. CECs, viable circulating endothelial cells (V-CECs) and CEPs were measured by six-color flow cytometry. CECs and circulating endothelial progenitor cells (CEPs) values change after cycles of chemotherapy. Among the patients, 22 patients were examined within 7 days prior to chemotherapy, twice a week during first and second cycle chemotherapy, then once a week at subsequent cycles of chemotherapy. When analyzing, point of measurement were divided into Day 1 of chemotherapy, 1st week of chemotherapy and after 1st weeks of chemotherapy. The Day 1 of chemotherapy was set as reference point.

Results: There were total 36 courses of chemotherapy for the 15 patients included in our study. The means of CEC, V-CEC 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/µL, 95% CI = (-3.98,-1.25); -1.57/µL, 95%CI = (-3.00,-0.14); and -4.01/µL, 95% CI = (-6.69,-0.32) respectively. After 1st week of chemotherapy and prior to 2nd week of chemotherapy, the means of CEC, V-CEC, and CEP came back to a similar level compared to Day 1 of treatment. The differences were 0.07/µL, 95%CI = (-1.71,1.85); 1.11/µL, 95%CI = (-4.91,1.70); and -0.39/µL, 95% CI = (-0.54,-0.16) respectively. There is a trend towards increase in total number of CEC 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 progression needs further studies.

Disclosure: All authors have declared no conflicts of interest.

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.

Disclosure: All authors have declared no conflicts of interest.
Results: Our study included 1752 patients of which 75 developed brain metastasis. The 5-year BFS was 84.5% for ER-ve, 86.4% for PR-ve, 84.2% for HER2-neu-ve patients compared to 93.5% for ER+ve (p<0.001), 93.7% for PR+ve (0.006) and 92.5% for HER2-neu+ve patients (0.002). Patients with grade III tumors had a lower BFS of 81.2% compared to 91.1% for those with grade I disease (p<0.001). Positive lymph nodes had a marginal significance of a lower BFS as well (90.2% vs. 94.5%; p=0.042). There was no significant difference seen according to age, pathological type or menopausal status. In a multivariate analysis model, histological grade one 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 BFS 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 BFS 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.

246P 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: 1996-2006). Clinicopathological 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 ±S.D. follow-up 30 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), (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<0.001), pN (HR 3.05, p<0.005), 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 outcome.

Disclosure: All authors have declared no conflicts of interest.

247P LOW EXPRESSION LEVEL OF NUCLEOSTEMIN (GNN3), STIMULATOR OF CANCER STEM CELL CELL FEATHER, IS A PROMISING BIOMARKER TO PREDICT PATHOLOGIC COMPLETE RESPONSE (PCR) IN NEOADJUVANT TREATMENT WITH BREAST CANCER

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Background: Both nucleostemin (GNN3) and guanine nucleotide binding protein-like 3 (GNN3L) are interacting proteins with human telomerase reverse transcriptase (hTERT). These proteins promote cell proliferation and tumorigenicity in vivo, and up-regulate CD44 and CD133 which are already established marker for cancer-stem cell, in the GNN3/GNN3L transfected cells. Thus, both GNN3 and GNN3L are considered as “cancer stem cell initiator” and novel therapeutic molecular targets.

Methods: We have conducted a prospective phase II trial in neoadjuvant setting with operable or locally advanced breast cancer. Eligible criteria include, stage IIA-IIIC, chemotherapy-naive, measurable disease, age ≥ 20, PS 0 or 1, and adequate organ function. Patients were treated preoperatively with four cycles of fluorouracil / epirubicin / cyclophosphamide (FEC) (500 /100/500 mg/m2) followed by 12 cycles of weekly paclitaxel (80 mg/m2) with or without trastuzumab (2mg/kg; with a loading dose of 4 mg/kg). mRNA levels of both GNN3 and GNN3L were evaluated by real time RT-PCR.

Results: Between December 2007 and February 2010, one hundred and forty five patients were enrolled in the prospective study. Sixty eight primary cancer tissues before the treatment by needle biopsy are available. Sufficient mRNA for real time RT-PCR was extracted in 53 cases. Pathological responses have been fixed in 34 cases out of them at the point on April 2010. Median age was 47. PS 0/1: 29/5; Stage IIA/IIIB/IIIC: 8/16/4/2; HER2 positive/negative: 10/24; Hormone receptor positive/ negative 12/22; Historical grade 1/2/3: 1/14/19. pCR rate was 29.4%. Expression of GNN3 have correlated with that of GNN3L (R=0.78). Low expression of GNN3 have statistically correlated with pCR (p<0.018) by ANOVA test.

Conclusions: Our results indicated that there are chemo-resistant populations with breast cancer stem cells in operable breast cancer. Low expression of GNN3 is a promising predictive marker of pCR in neoadjuvant treatment with breast cancer. This is the first report that expression of GNN3 correlated with chemo-resistant in clinical study.

Disclosure: All authors have declared no conflicts of interest.

248P 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. 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 Clinic of 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.
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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%, IIIA 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 to 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 multivarient 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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Background: The 70-gene tumor expression profile “MammaPrint” was established as a powerful predictor of disease outcome in breast cancer. The St Gallen 2009 recommendations include gene expression signatures as an indicator for adjuvant therapy. Here we determined in an Italian cohort how the 70-gene profile could assist in patient management.

Methods: Fresh tumor samples (n=584) from breast cancer patients (clinical T1-4N0-3M0) aged 26 to 98 years (median age 63 years), were collected in 12 Italian hospitals in 2008 and 2009 by core needle biopsy or from a surgical specimen (study protocol MP 000). We assessed agreement between the treatment advice as recommended by the 2009 St Gallen Highlights and classification according to the 70-gene MammaPrint profile.

Results: According to the St Gallen 2009 treatment recommendations, 4 patients could forgo any adjuvant treatment (<1cm, LNO, PVI0). Of these patients, 3 were classified to be poor prognosis signature by MammaPrint. Another 17 patients with tumors <<1cm, LNO, PVI= are ER= and are recommended endocrine treatment, of whom 9 are MammaPrint high risk. The 126 Her2+ patients would be recommended anti-Her2 treatment as well as adjuvant chemotherapy according to the 2009 recommendations. Of these patients, 19 (15%) were classified as good prognosis signature by MammaPrint. All 47 (ER=) patients who are recommended chemotherapy alone are classified as poor prognosis by MammaPrint. For the 389 ER+ patients, HER2- patients, 17 would be recommended no adjuvant chemotherapy (Grade I and LN0 and ER+ and ER50%) and 199 would be recommended adjuvant chemotherapy being either Grade III, or 4LN, or >5cm, or ER=50%. Of these 215 patients, 73 (34%) are classified as low risk by MammaPrint. The remaining 174 ER+, HER2- patients fall in the subgroup for which St Gallen 2009 states that they have characteristics that are not useful for decision making; MammaPrint classified 101 (58%) as poor prognosis and 73 (42%) as good prognosis.

Conclusion: For the majority (93%) of these 584 breast cancer patients from 12 Italian community hospitals, the St Gallen 2009 other recommends or suggests adjuvant treatment with cytotoxic adjuvant therapy for whom MammaPrint indicates a low risk of recurrence in 30% of cases.

Disclosure: All authors have declared no conflicts of interest.
success of breastfeeding. Acknowledging the small sample size, breastfeeding does not seem to affect the prognosis of these women. Proper fertility and survivorship counselling is crucial and requires more attention in breast cancer clinics.

Disclosure: All authors have declared no conflicts of interest.

EARLY OSTEOPOROSIS RISK IN PREMENOPAUSAL WOMEN WITH BREAST CANCER AFTER OVARIAN ABLATION

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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.

Materials and methods: The study group consisted of 34 premenopausal women with breast cancer. The diagnosis was histopathologically proven and hormone receptors were positive in all patients. Control group consisted of 15 healthy individuals. 18 patients were observed over 2 years, 16 patients were observed over one year. Ovarian ablation was made in 7 of 34 patients by chemotherapy, and in 27 of 34 patients by hormone therapy. The levels of baseline, sixth month, first year, and second year of calcium, phosphate, ionized calcium, ALP, FSH, LH, estradiol, osteocalcin, osteoprotegerin, osteocalcin, and PTH were obtained. Lumbar spine and femur bone mineral density was measured.

Results: The measurements of patients and control groups in baseline counts 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, osteocalcin and osteoprotegerin levels. However, osteocalcin levels were significantly increased at second year (P<0.004). Levels of estradiol were significantly decreased at sixth month, first year and second year (P<0.001). When compared with the basic measurement there was a statistically significant decrease in L1-4 bone mineral density of at 6th month, 1st year, 2nd year (P<0.001). There was a statistically significant decrease in T score of femur neck between baseline and sixth month and second year (P=0.038). While none of the patients had osteoporosis at the beginning, at the end of 1st year one patient and at the end of 2nd year 3 of 18 patients had osteoporosis. Among patients observed through one year only one patient had developed osteoporosis.

Conclusion: Ovarian insufficiency caused by hormone therapy may result in osteoporosis. Further studies should be performed to evaluate the increase in bone mineral density. 10% of patients undergo ovarian ablation; these patients must be followed closely due to these risks.

Disclosure: All authors have declared no conflicts of interest.

TRASTUZUMAB AS ADJUVANT THERAPY IN HER2+ EARLY BREAST CANCER – CARDIAC SAFETY ANALYSIS

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Background: Trastuzumab (T) is effective in human epidermal growth factor receptor 2-positive (HER2+) breast cancer (BC), but it increases frequency of cardiac dysfunction (CD) when used with or after anthracyclines. Purpose: To assess cardiac safety of T in the adjuvant treatment of BC at Instituto Português de Oncologia do Porto.

Material and methods: Patients (pts) with HER2+ early BC treated with fluorouracil, epirubicin and cyclophosphamide followed by docetaxel (FEC-D) plus 1 year of T as adjuvant therapy, from 11.07 to 06.09, were included in this retrospective study. Descriptive analysis of clinical and treatment data was performed. Left ventricular ejection fraction (LVEF) was assessed by multiplanar acquisition scan or echocardiogram. Cardiac events (CE) were reviewed and an association with risk factors was tested using Fisher’s exact test and univariate log-rank analysis.

Results: Of 96 HER2+ pts treated with FEC-D, 88 received T (66% sequential, 34% concurrent). Median follow-up from T was 9 months (0-22). Median age was 53 years (24-71) and 24% had stage III disease (10% were hormone receptor (HR)-positive (HR+)/HER2+ BC patients were enrolled in the study. The rate of CD occurring in the first year of T was 12%. At any time of follow-up, the rate of CD was 18%.

Conclusion: HER2 overexpression and amplification have been correlated with shorter disease-free survival and overall survival in BC pts. The rate of CD occurring in the first year of T was 12%. T appears to be safe and well-tolerated in early BC patients with HER2+ breast cancer. The rate of CD occurring in the first year of T was 12%.

Disclosure: All authors have declared no conflicts of interest.

DOES ADJUVANT CHEMOTHERAPY BENEFIT PATIENTS WITH NODE-POSITIVE, HORMONE-RECEPTOR POSITIVE, AND HER2 NEGATIVE BREAST CANCER?

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Background: The benefit of adjuvant chemotherapy (Ca) is proved in non-selected node-positive (N+) breast cancer (BC) patients (pts). However, recent studies have suggested that its benefit may be limited in hormone-receptor positive and HER2 negative (HR+/HER2-) BC patients, and endocrine therapy (Ex) alone is listed as an option for recommendation for the intermediate risk HR+/HER2- BC according to St. Gallen guideline (2007). Therefore, we performed an institutional-based review to investigate the impact of omitting Ca on clinical outcome in HR+/HER2- BC pts.

Methods: Patients included in this study were as follows: node-positive breast cancer patients who received breast surgery between 2001 and 2009 at the National Cancer Center Hospital; patients pathologically proven hormone-receptor positive and HER2 negative BC; patients who received Ex, Ca, or Ex+Ca. Disease-free survival (DFS) was compared to identify the benefit of Ca by Kaplan-Meier method.

Results: There were 412 patients included in this analysis. The median age was 55 (24-89). Of these, 308 (75%) patients had 1-3 lymph node metastases (intermediate risk in St. Gallen 2007 risk categories), and 104 (25%) patients had more than 4 lymph node metastases (high risk). In the intermediate risk group, 229 patients received Ex+Ca and 79 patients received Ex alone. The DFS at 5 years in patients who received Ex+Ca and Ex alone was 87% and 91% at a median follow-up period of 45 months (3-97)

Disclosure: All authors have declared no conflicts of interest.
FEATURES OF RECURRENTENCE 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 aggressive 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 18.4%(40) patients had recurrences with an average age of 52.5(±9.3) 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 60%(24) respectively for patients with recurrence. The most frequent involved organs with recurrence were visceral (lung and liver) 37.5%(15), bone 25%(10), skin 20%(8), CNS 12.5%(5) and contralateral breast 5%(2). Additionally we found five patients with history of familiar BC, and four of them were stage II with negative lymph node at diagnoses.

Conclusion: TN-NMBC are 26.0% 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 familiar 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 has 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 (15-86 y), 31 patients were younger than 40. The tumours were typically invasive ductal carcinoma (80%) with high histological grade (93.6%). According to stage: St I/II/III 31%(46.7%)22%. Lymph node metastasis was present in 41%. Pathologic report described neoplastic (71%), lymphocyte infiltration (8%), extensive vacuolar 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) has 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. Although previous experimental studies have indicated that tumors with BRCA1 mutation are less sensitive to taxanes, it remains to be clinically determined whether TNBCs are sensitive to taxanes.

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 epirubicin (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 anthracyclines and 3) after taxanes. A total of 71 patients fulfilled the eligibility criteria for this study. We compared the clinical responses of TNBC to taxanes with that of non-TNBC.

Results: 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 anthracycline. No tumor progression while receiving taxanes occurred in the patients with non-TNBC.

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

Disclosure: All authors have declared no conflicts of interest.

FACTORs 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 99mTc-Antimony sulfide colloid.

Methods: 250 consecutive patients with the diagnosis of early stage breast cancer were searched. 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, 0.35 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: Most often, the pathologist when evaluating a small core biopsy specimen may realize that the lesion is not fully sampled. In these circumstances, a decision is made to excise the lesion from the breast. In this situation, an excisional biopsy is performed.

Methods: When a sentinel biopsy is performed, the specimen is sectioned in thin slices, usually 5 mm thick, and examined under the microscope. By reviewing the sections, the pathologist will determine if the lesion is adequately sampled or if the lesion is not present in the specimen. If the lesion is not fully sampled, a decision is made to perform an excisional biopsy.

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, 0.35 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.
PHASE II STUDY OF DOCETAXEL AND DOXORUBICIN COMBINATION AS NEOADJUVANT CHEMOTHERAPY IN OPERABLE BREAST CANCER PATIENTS

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Patients and methods: Thirty-eight women were treated with intravenous doxorubicin 50 mg/m2 over 15 min followed by a 1-h infusion of docetaxel 75 mg/m2 every 3 weeks. Dexamethasone and anti emetic drugs as premedication was allowed.

Background: The idea of using neoadjuvant chemotherapy in patients with operable breast cancer is dated from experimental and clinical observations as well as from theoretical hypotheses on tumor cell growth and dissemination. Several recently reported trials of neoadjuvant therapy incorporating newer agents such as taxanes in breast cancer 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.

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 93% (95% confidence interval (CI) 75% to 95%) in the evaluable population (n = 37). Disease-free and overall survival rates were 83% (95% CI 71% to 94%) and 96% (95% CI 85% to 99%), respectively, after a median follow-up of 16 months. Grade 3/4 neutropenia was observed in 46% of patients and 13% reported grade 4 febrile neutropenia.

Conclusion: Docetaxel and doxorubicin is an effective and well-tolerated regimen for locally advanced disease, however further studies are needed to explore the role of combination therapy in patients with early breast cancer and in patients with locally advanced disease.

Disclosure: All authors have declared no conflicts of interest.

PREGNANCY AND BREAST CANCER

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Background: Choice of 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 1997-2009. In 29 patients tumor was detected during pregnancy, in 58 – during lactation (first months after childbirth). In 37 (42.5%) patients early BC (T1–N0–M0) was detected, in 22 patients – locally-advanced BC (T3–N1–M0), 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 (75.9% 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>0.50). 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.

MALE BREAST CANCER


Radiotherapy, INO, Rabat/MOROCCO

Background: Male breast cancer is rare; it constitutes 0.2–1.3% of all malignnant 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 evolutive 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, and 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% of 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 with or without chemotherapy. It was possible to follow up 100 of the patients. The median of follow-up was 49 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 (33% 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.

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 17-α-hydroxyprogrenolone (17-OHP) pathway.

Patients and methods: Breast cancer patients that had been treated with AIs for 12–48 months were included. Serum androstenedione, DHEAS, 17(OH) progesterone, 17α–hydroxyprogrenolone and a 24 hr urinary free cortisol were measured. Also the bone formation marker procollagen I propeptide (PINP) and bone resorption marker, type 1 collagen amino telopeptide (NTx) were measured. Urinary NTx was correlated with 24 hr urinary cortisol free by linear regression analysis.

Results: From October 2008 and January 2010, 19 patients were enrolled on the trial. Data analysis was in May 2010. No statistically significant alteration occurred in the levels of androstenedione, DHEAS, 17(OH) progesterone, 17α–hydroxyprogrenolone and 24 hr urinary free cortisol, however individual variations of importance were observed. In a study of the correlation between urinary NTx and 24hr urinary free cortisol no correlation was initially found (Results A). In a retrospective review patient 82 was excluded due to probable occult bone metastasis at accrual; violating the inclusion criteria (compression fracture L5 spine on x-ray, 8 month Hx bilateral leg pains, highest Ur. NTx/Cr (86 nMol BCE/mmol) and PINP (814 μg/L) of accrued

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Disclosure: All authors have declared no conflicts of interest.
preferred dose of tamoxifen (20 mg) was administered daily in 39 patients with invasive lobular carcinoma who underwent surgery 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 micro-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 51 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-mm-thick serial sections were treated with the following polyclonal antisera: VEGF-R1, CD 133, CD 117, CD-34. CD34 and CD117 appeared as the most useful HPCs markers, whereas Rh−1 and CD133 exhibited a variable rate of immunostained elements. After a median follow-up of 62.6 months (6–136), 29 pts are positive in 28. Three hundred and 47 patients received surgery for localized disease. Median age was 32 years. Fifty three patients (13%) had metastatic disease at the time of surgery. Three hundred and 56 patients (87%) had localized disease. Twenty-eight 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 = 2.42, 95% CI = 1.23–4.66, 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).

Conclusion: 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.
Background: Survival, dramatically overexpressed in most human cancers, is an important nodal protein involved in multiple signalling mechanisms in tumor maintenance and in apoptosis inhibition. Testin (TES) is a tumor suppressor gene, that was reported to be altered in leukemia, lymphoma and breast cancer cells and probably have a prognostic value in some tumors, especially in head and neck carcinoma and prostate cancer. In a previous experimental study we have demonstrated a possible relationship between the expression of TES and the proliferation of apoptosis in different tumor cell lines, included breast cancer cells. The prognostic potential of TES downregulation and survivin overexpression was investigated in a series of 121 operable primary breast cancer.

Material and methods: Using archived tumor tissue from 121 patients, diagnosed with stage I-II primary breast cancer between 2000-2008, we determined the expression of TES and survivin by immunohistochemistry. Invasive ductal carcinoma was found to be the most prevalent breast cancer type. Median follow up and age were 48 months and 53 years, respectively. All patients underwent surgery a radiotherapy and systemic standard treatment. Statistical analysis was applied to all patients and was performed using SPSS software.

Results: The TES expression is high in normal mammary epithelium and decreases in breast tumors, unlike survivin. Cytoplasmatic positivity for survivin and TES was observed in 98% and 58% of tumors, respectively. Survivin nuclear positivity was in 35.5% of samples. Patients with absence or low TES showed a tendency toward long distant metastasis and/or contralateral tumor, but this correlation has to be confirmed using a large sample size (about 300 patients will ensure a 80% power). Nuclear localization of survivin is significantly correlated with local recurrence (p < 0.002).

Conclusions: Our preliminary data could provide valuable information that high nuclear expression of survivin may be predictive for early local recurrence and suggest that TES should be a new prognostic factor in early-stage breast cancer. However, the results are not conclusive and further investigation is required to confirm their role.

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