The Breast 22S1 (2013) S71–S120

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Poster Abstracts II

Surgery/Sentinels/DCIS

P160

PRE-OPERATIVE ASSESSMENT OF AXILLARY LYMPH NODES IN PATIENTS WITH EARLY BREAST CANCER

A.M. Huws*, I. Patchell, S. Khawaja, K. Nadi, S. Khaliq, G. Dazeley, A. Barnett, Y. Sharaiha, S.D. Holt. *Department of Surgery, Prince Philip Hospital, Llanelli, United Kingdom*

Goals: Preoperative assessment of patients with breast cancer requires clinical examination and imaging of the axilla, best performed with ultrasound. Nice (2009) guidelines recommend preoperative sonographic imaging of the axilla in patients with breast cancer. The primary aim of the study was to determine the impact of preoperative FNAC/Core biopsy of axillary lymph nodes on re-operation rates for positive sentinel nodes. In addition retrospective review of histological features was undertaken to ascertain whether there were any predictive factors for lymph node involvement.

Methods: All patients in our institution requiring axillary node clearances (AC) after sentinel node biopsy (SNB), between August 2008 and August 2011, were identified. The imaging, clinical records and histology reports of cases were reviewed retrospectively. Additional data collected from the preoperative core biopsy histology and final histology included: ER, PR, Her-2 status; tumour size; tumour grade; tumour type; presence of lymphovascular invasion; presence of multifocality; and final lymph node status.

Results: A total of 663 patients were identified. Of these, 190 patients were listed for SNB. 59 patients required AC. The overall rate over the 3 year period of patients undergoing an AC following a SNB was approximately 31.05%. Between 2010 and 2011 the unit performed imaging in all patients listed for SNB, reviewing the axillae preoperatively and the rate of SNB to AC in this final year was 29.23%. In the cohort requiring AC after SNB, the mean tumour size was 27 mm. The presence of lymphovascular invasion in this group, especially on final histology was 62.7%. The presence of multifocality was 15.8% overall. The majority of the tumours were grade 2 infiltrating ductal carcinomas, although there was a high incidence of grade 3 tumours of 22.03%. The percentage of tumour with ER positivity was 62.7%, although interestingly there was high incidence of progesterone receptor negativity, 35.5%. Her-2 status was similar to the general breast cancer population, being 13.56%. 58% of the patients with a positive sentinel node had only one lymph node involved after axillary clearance. On final comparison of the SNB-only group and SNB to AC group, the mean tumour size of the latter cohort was larger (27 mm vs. 16.2 mm); had a higher incidence of lymphovascular invasion (62.7% vs. 2.57%); more cases of multifocality (15.8% vs. 5.2%); higher rate of DCIS (42% vs. 39%) and PR negativity (31% vs. 26%).

Conclusion: This retrospective review suggests that patients with multifocal disease and larger tumour sizes on preoperative imaging require careful assessment and biopsy of any indeterminate nodes found on imaging. The presence of lymphovascular invasion on core biopsy suggests review of axillary imaging as its presence on preoperative histology is highly indicative of sentinel node involvement.

Disclosure of Interest: No significant relationships.

P161

THE EFFICACY OF ARM NODE PRESERVING SURGERY FOR PREVENTING LYMPHEDEMA IN BREAST CANCER

Su Hwang Kang*, J.E. Choi, S.J. Lee. *General Surgeon, Yeungnam University College of Medicine, Daegu, South Korea*

Goals: The axillary reverse mapping (ARM) technique to identify and preserve arm nodes during sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) was developed to prevent lymphedema. In our previous study, we evaluated the incidence of lymphedema after ARM and the difference in arm circumference between arm node preserved group and unpreserved group, after short term follow up. The purpose of this study was to investigate the location and metastatic rate of the arm node, and to evaluate the further follow-up results of the differences in arm circumference after arm node preserving surgery.

Methods: From January 2009 to December 2011, 116 breast cancer patients who underwent ARM were included. Blue-dye (2.5 ml) was injected into the ipsilateral upper-inner arm. At least 20 minutes after injection, SLNB or ALND was performed and blue-stained arm nodes and/or lymphatics were identified. Patients were divided into two groups, an arm node preserved group (87 patients had ALND, 10 patients had SLNB) and an unpreserved group (15 patients had ALND, 4 patients had SLNB). The difference in arm circumference between preoperative and postoperative time points was checked in both groups.

Results: The mean number of identified blue stained arm nodes was 1.41 ± 0.66. The mean follow up period was 16.24 (3–24) months. In the majority of patients (86.2%), arm nodes were located between the lower level of the axillary vein and just below the second intercostobrachial nerve. The location of the arm node was the inferolateral side of axillary and thoracodorsal vessels in 62 patients (53.4%), the inferomedial side in 46 patients (39.7%), the superolateral side in 5 patients (4.3%), and the superomedial side in 3 patients (2.6%) In the arm node unpreserved group, 5 patients (4.3%) had metastasis in their arm node. When comparing between arm circumferences in ipsilateral upper-extremity of the arm node preserved group and unpreserved group, in the SLNB group, there was no significant difference. But in the ALND group, the arm circumference changes of the arm node unpreserved group were bigger than that of the preserved group (0.50 ± 1.15 vs 0.16 ± 0.76, $p = 0.066$). There were no lymphedema cases among the arm node preserved group, but one lymphedema developed in the unpreserved group (5.2%). There was no locoregional recurrence in both group in follow up periods.

Conclusion: After further follow-up, this study showed some differences in arm circumference between two groups. Arm node

preserving was possible in all breast cancer patients with identifiable arm nodes, during ALND or SLNB, except for those with high surgical N stage, and lymphedema and locoregional recurrences did not develop in patients with arm node preserving surgery.
Disclosure of Interest: No significant relationships.

P162
SENTINEL LYMPH NODE EXAMINATION: RESULTS OF 3 DIFFERENT APPROCHES IN A SINGLE INSTITUTION

L. Di Tommaso[1]*, B. Fernandes[2], B. Fiamengo[2], P. Spaggiari[2], S. Manara[3], C.A. Garcia-Etienne[4], G. Masci[5], A. Testori[4], C. Tinterri[4], M. Roncalli[6]. *[1]Biotechnology and Translational Medicine, University of Milan, School of Medicine and IRCCS Humanitas Cancer Center, Rozzano (Milan), Italy, [2]Pathology, IRCCS Humanitas Cancer Center, Milan, Italy, [3]Pathology, IRCCS Humanitas Cancer Center, Milan, Italy, [4]Breast Surgery Unit, IRCCS Humanitas Cancer Center, Milan, Italy, [5]Oncology, IRCCS Humanitas Cancer Center, Milan, Italy, [6]Biotechnology and Translational Medicine, University of Milan, School of Medicine, Milan, Italy*

Goals: To test the diagnostic accuracy of a novel molecular procedure of sentinel lymph node (SLN) evaluation, namely OSNA (One-Step Nucleic Acid Amplification), against well standardized morphological procedures of SLN evaluatiopn either performed on formalin fixed paraffin embedded tissue (FFPE) or on frozen section (FS).
Methods: We evaluated the clinical-pathological features of three series of SLN-patients from a single Institution. The series consists of 540 FFPE (2000–2005), 390 FS (2009) and 437 OSNA (october-2011 to september-2012) patients.
Results: Positive SLN were disclosed in 162/540 (30%) FFPE, 87/390 (22%) FS and 119/437 (27%) OSNA and represented by metastases-micrometastases [FFPE: 61%-38%, FS: 74%-26%, OSNA: 68%-32%]. After axillary dissection, additional metastasis were observed in 53/162 (33%) FFPE, 27/87 (31%) FS and 40/117 (34%) OSNA patients, with further involvement more frequent with metastasis (FFPE 43%, FS 36%, OSNA 43%) rather than micrometastasis (FFPE 16%, FS 17%, OSNA 16%). No statistical difference were obsereved among the three series.
Conclusion: OSNA provides results overlapping to those of FFPE and FS, thus representing a valid and objective alternative for intraoperative SLN examination in breast cancer.
Disclosure of Interest: No significant relationships.

P163
COLOR DOPPLER ULTRASONOGRAPHY IN CLINICALLY NODE NEGATIVE BREAST CARCINOMA: OUR EXPERINCE

N. Singh*. *Surgery, St Josephs Hospital, Lucknow, India*

Goals: To find an easy method for deciding on axillary lymph node dissection in clinically node negative breast carcinoma patients, as our center does not have nuclear medicine facilities to detect sentinel lymph nodes of the axilla.
Methods: A preoperative duplex ultrasonography (USG) of all clinically node negative breast carcinoma patient was done. Parameters evaluated were: Long/short axis ration, flow pattern, resistivity index and pulsatility index. Axillary dissection was done and the histopathology results were compared with the preoperative findings of USG.
Results: In the study 25 patients were evaluated. Mean age of the patients was 47.02 years. Mean number of nodes detected on USG more in case of patients with nodal deposits (2.818 ± 0.603) as compared to patients who had no lymph node metastasis (1.428 ± 0.514). Flow pattern had a sensitivity and specificity of 82.7% and 90.9% respectively.
Conclusion: Color Doppler USG examination of axillary lymph nodes is a cheap and easy available facility with good patient compliance. In clinically node negative breast carcinoma patients it can help delineate a group of patients who can be spared from axillary dissection and can be followed up regularly.
Disclosure of Interest: No significant relationships.

P164
BREAST CANCER PRESENTING AS AXILLARY MASS: REPORT OF FIVE CASES

Sun Hee Kang*. *General Surgery, Keimyung University School of Medicine, Daegu, South Korea*

Goals: Occult primary breast cancer is isolated axillary adeno-carcionma without detectable tumor in the breast by either physical examination or breast image test. With progress in diagnostic imaging equipment, occult breast carcinoma was increased incidentally. We report five cases of occult breast cancer in which the primary site could not be identified on breast imaging tests.
Methods: From January 1991 to December 2012, two thousand one hundred twenty patients were diagnosed with breast cancer and underwent breast surgery at our institution. We retrospectively reviewed medical records and found five patients who presented breast carcinoma as axillary lymph node enlargment with no clinical evidence of a primary tumor. We excluded patients which were found primary breast lesion on final pathologic results. All patients were evaluated with a physical examination, MMG and USG. Four patients underwent breast MRI and three underwent PET CT scan. Radiologist applied BIRADS system on description of imaging results. The methods of pathologic diagnosis of aillary lymph node were fine needle aspiration or core needle biopsy or excisional biopsy.
Results: The ages ranged from 44 to 62 years with a mean age of 52.4 years. Four of five patients presented symptom with a painless palpable mass at axilla, one patient was found axillary lymph node enlargement by PET-CT scan during evaluation of rectal cancer. Preoperative image study including USG, MMG, MRI showed no sign of malignant lesion in both breast. All patients were underwent level I, II axillary node dissection. Their pathologic results are described in Table 1. All of patients were given adjuvant chemotherapy, however, none of them did receive whole breast radiation therapy or mastectomy. Median follow up period is 44 months (range 3–229 months), they did not show any sign of intra-breast tumor recurrence or distant metastasis. They were alive and remained free of disease at the end of the follow up period.

Table 1. Pathologic result of five patients

Case	Operation year	Pathology (No. of metastatic LN)	TNM	ER	PR	HER2
1	2012	Metastatic ca, primary in breast (5/38), internal mammary lymph node metastasis (1/1)	T0N3M0	–	–	1+
2	2012	Metastatic ca, primary in breast (2/45)	T0N1M0	–	–	3+
3	2011	Metastatic ca, primary in breast (2/29)	T0N1M0	–	–	1+
4	2009	Metastatic ca, primary in breast (1/19)	T0N1M0	–	–	3+
5	1991	Metastatic ca, primary in breast (26/26)	T0N3M0	?	?	?

?, unknown.

Conclusion: We did not mastectomy nor whole breast radiation therapy in patients with axillary presenting breast cancer. During follow up period, none of them recur in the breast. If MRI and PET-CT show no evidence of primary lesion in breast, we can consider to omit the breast treatments.
Disclosure of Interest: No significant relationships.

P165
SLNB AFTER NEOADJUVANT CHEMOTHERAPY WITH CYTOLOGICALLY PROVEN AXILLARY NODE METASTASIS

M. Kim*, J. Kim, J. Lee, S.Y. Bae, H. Baek, W.H. Kil, J.E. Lee, S.J. Nam. *Surgery, Samsung Comprehensive Cancer Center, Seoul, South Korea*

Goals: The role of sentinel lymph node biopsy (SLNB) in locally advanced breast cancer patients after neoadjuvant chemotherapy (NAC) is still controversial. It has been known that the response to

NAC may be different according to the molecular subtypes of the primary tumor. In this context, we performed sentinel lymph node biopsy in patients treated with NAC with cytologically confirmed axillary lymph nodes metastases at presentation. We analyzed the relationship of molecular subtypes and the feasibility of SLNB as well as pathologic responses in the breast and axillary nodes after NAC.

Methods: We retrospectively evaluated 47 patients with invasive breast cancer with ultrasound-guided fine needle aspiration-proven axillary nodal metastases at the time of diagnosis, who underwent SLNB after receiving NAC at Samsung comprehensive cancer center between Jan 2006 and Dec 2012. In these patients with proven metastasis we analyzed the breast and axillary responses on molecular subtypes.

Results: Sentinel node identification rate was 97.9% (46/47), presenting false-negative rate for SLNB after NAC of 8.7% (2/23). Median number of sentinel lymph nodes retrieved was 2 (range 1–10). Post-NAC sentinel lymph nodes of 9 patients (39.1%) are the only nodes containing residual axillary metastases. Of these 47 patients, pCR of the primary breast tumor and axilla was achieved in 10 patients (21.3%). Twenty four had an axillary pCR (51.1%) and 11 patients achieved breast pCR (23.4%). Fourteen of those patients achieved axillary pCR (14/24) did not accomplish breast pCR. Ten of the patients who had a pCR of the primary tumor (10/11) achieved axillary pCR. On the analysis by subtypes according to receptor status, five achieved an axillary pCR among 14 ER+/HER2− patients (35.7%). Of 19 HER2+ patients and 14 triple negative patients, an axillary pCR was achieved 12 (63.1%) and 7 (50.0%), respectively. Breast pCR was achieved in 7 HER2+ patients (36.8%), in 4 triple negative patients (28.6%), and no one achieved breast pCR in ER+HER2− patients. The median follow-up was 7 months (range 1–56) with 6 events; 1 local recurrence on operation bed in a HER2+ patient, 2 regional nodal recurrences occurred in ipsilateral supraclavicular nodes in triple negative and HER2+ patients, 2 systemic recurrences in an ER+HER2− and triple negative patients, and 1 contralateral breast cancer occurred in a triple negative patient. Among them five were non-pCR patients and one showed axillary pCR but residual tumor in breast.

Conclusion: The post-neoadjuvant chemotherapy sentinel lymph node biopsy in patients with cytologically documented breast cancer axillary metastases is feasible. The axillary pCR rate is higher in subgroups with HER2 positive tumors and triple negative tumors. In those patients axillary clearance could be avoided through sentinel lymph node biopsy.

Disclosure of Interest: No significant relationships.

P166

INTERPECTORAL ROUTE OF AXILLARY LYMPH NODE DISSECTION IN BREAST CANCER – A NOVEL TECHNIQUE

V.S. Chauhan *. *Surgery, Metro Hospital, Faridabad, India*

Goals: Level 3 Axillary nodal clearance during modified Radical Mastectomy in Carcinoma Breast is done conventionally by retracting the pectoralis minor muscle medially and exposing the Axillary vein. However, we have been performing the level 3 clearance by retracting the Pectoralis minor muscle laterally and entering the interpectoral groove.

The aim of the study was to compare the nodal yield and efficacy of technique of level 3 axillary nodes using the conventional subpectoral route and the Interpectoral route.

Methods: The study was done at Metro Hospital, Faridabad, India. A total of 80 females were enrolled in the study. All these females underwent Modified Radical mastectomy at the hospital. However 40 females each underwent Level 3 Axillary lymph node dissection using the Conventional Subpectoral approach or the Interpectoral approach. Level 3 Nodal yield, pain scores, Length of stay and duration of Axillary drain were compared statistically.

Results: A total of 80 females with carcinoma Breast were enrolled in the study and were randomly allocated to the Subpectoral and Interpectoral Axillary clearance group with 40 patients in each. The nodal yield was 22% higher in the interpectoral group as compared to the Subpectoral group which was statistically significant. The number of complications was lower in the subpectoral group. However, five patients required prolonged Axillary drainage for more than 3 days.

Conclusion: Level 3 Axillary clearance using Interpectoral approach gives a better nodal yield and less complications as compared to the Subpectoral approach.

Disclosure of Interest: No significant relationships.

P167

PERIAREOLAR APPROACH IN VIDEO-ASSISTED BREAST SURGERY AND AESTHETICS IN SKIN-SPARING MASTECTOMY

K. Yamashita[1] *, K. Shimizu[2], S. Haga[1]. [1]*Department of Breast Surgery, Nippon Medical School, Bunkyo-ku, Tokyo, Japan,* [2]*Department of Endocrine Surgery, Nippon Medical School, Bunkyo-ku, Tokyo, Japan*

Goals: Early-stage breast cancer patients, such as DCIS, may be forced to remove the whole mammary gland due to their wide-range extension of cancer cells in the ducts. In such early cases, skin-sparing mastectomy (SSM) should be recommended. However, the traditional techniques leave ugly scars on the breast subjected to a large skin incision. The degree of satisfaction will be failing lower. By applying the technique of endoscopic video-assisted breast surgery (VABS), we can perform SSM only with the skin incision at the edge of the areola, which can leave no scar on the breast, and can provide a better aesthetic surgery for breast cancers.

Methods: The sentinel node biopsy was subjected to a 1 cm incision in the axillary position which was marked with a 3D-CT mammary lymphangiography prior to surgery. We inserted Visiport (optical trocar), which can detect sentinel nodes stained with blue dye endoscopically. SSM is started from the skin incision of 2.5–3.5 cm long at the foot-side of the edge of the areola, to preserve blood flow around the areola. Subsequent performance was carried out under endoscopic view only from the periareolar port. Lap-protector for breast surgery was inserted to protect the wound margin. After peeling around the total circumference of the mammary gland neck under the areola, we have to cut across the gland and quickly submit the transected stump of the gland as a sample of the nipple side margin to the pathological department to make certain of negative margins. We made a skin flap over the whole gland subcutaneously by the tunnel-method, and peeled the gland just above the pectoralis major muscle fascia. And the whole gland was liberated, and was excised from the port. Simultaneous reconstruction was carried out by inserting implants under the pectoralis major muscle pocket.

Results: We have performed VABS on 300 patients from 2001, and underwent SSM by VABS on 20 patients with no cancer progression to the skin. Tumor size was 1.6 cm on average. Age was 57.2 years. We can preserve the nipple-areolar complex on 13 patients. There was DCIS in 12 cases, two invasive lobular carcinoma, six invasive ductal carcinoma. There was SN metastasis in two cases, and the other axillary metastasis in one case. It is important to care the performance near the skin, which was protected with the retractor with suction. There was no difference in blood loss and operation time. The simultaneous breast reconstruction made the best aesthetic performance which brought high satisfaction with less sensory disturbance and no skin scar on the breast. After 38 months, there have been no distant metastases, no postoperative deaths, and one local recurrence, which was excised locally.

Conclusion: Periareolar-edge approach in endscopic video-assisted breast surgery (VABS) makes better aesthetic results in skin-sparing mastectomy for early-stage breast cancer.

Disclosure of Interest: No significant relationships.

P168
SNB AFTER NAC IS ACCURATE IN BREAST CANCER PATIENTS WITH A CLINICALLY N0 BEFORE NAC

Y. Kajiwara[1] *, M. Kochi[1], M. Kohno[2], M. Ito[3], S. Ohtani[1], K. Higaki[3]. [1]*Breast Surgery, Hiroshima City Hospital, HIroshima, Japan,* [2]*Medical Oncology, Hiroshima city hospital, Hiroshima, Japan,* [3]*Department of Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan*

Goals: Sentinel lymph node (SLN) biopsy in early breast cancer is widely used as a standard treatment. However, SLN biopsy after neoadjuvant chemotherapy (NAC), which is also widely used to enable a breast conserving surgery, is still investigational. The aim of this study was to evaluate the accuracy and feasibility of SLN biopsy after NAC.
Methods: From April 1999 to December 2009, 275 patients with advanced breast cancer were studied prospectively. Before surgery, all of them underwent NAC. At surgery, SLN biopsy followed by axillary lymph node (ALN) dissection was performed. The SLN was identified by the combined method that used the 99mTc-phytate and Indigocarmine. On the contrary, 2340 patients with clinically lymph node negative breast cancer underwent SLN biopsy as a standard treatment from 1999 to 2009.
Results: The SLN identification rate after NAC was 89.1% (245/275). False-negative rate was 9.7% (6/62). In N0 patients who are clinically lymph node negative before NAC, the SLN identification rate was 92.7% (76/82). Of note, the false-negative rate was 0% in N0 patients. In N1-N2 patients who are clinically and pathologically lymph node positive before NAC, the SLN identification rate was 87.6% (169/193), and the false-negative rate was 10.2% (6/59). On the contrary, the SLN identification rate without NAC was 94.8% and false-negative rate without NAC was 3.2%. The SLN identification rate and false-negative rate after NAC do not differ from those obtained in the case of early breast cancer without NAC. When the SLN couldn't be identified, ALN metastasis rate after NAC was 39.0% and that without NAC was 25.8%.
Conclusion: Our results show that SLN biopsy after NAC can be feasible and predict the ALN status with a high accuracy in patients who are clinically lymph node negative before NAC.
Disclosure of Interest: No significant relationships.

P169
SENTINEL NODE METASTASIS IS CORRELATED WITH TUMOR SIZE AND HISTOLOGICAL TYPE, BUT NOT WITH SUBTYPE

Y. Koyama *, E. Sakata, K. Tatsuda, M. Hasegawa, C. Toshikawa, N. Manba, M. Ikarashi. *Division of Digestive & General Surgery, Niigata University Graduate School of Medical & Dental Sciences, Niigata, Japan*

Goals: Sentinel node biopsy (SNB) for clinically N0 breast cancer has already become a standard procedure, however, it has been reported that SN metastasis was observed in about 25% cases. Some clinicopathological factors such as tumor size or nuclear grade have been recognized as predictive factor for SN metastasis, and recent reports have described the relationship between molecular subtype classification and SN metastasis. The aim of this study was to elucidate the validity of preoperatively available clinicopathological factors including subtype classification to predict the SN metastasis.
Methods: The invasive breast cancer patients who have received SNB at Niigata University Hospital between January 2003 and April 2012 were entered. The relationship between SN metastasis and clinicopahological factors such as pathologic tumor size, preoperative T-stage, histological type, nuclear grade, lymphatic and/or venous involvement, ER and/or PgR status, Her2 status, and subtype classification were examined. Statistical analyses were performed using Mann Whitney's U test and Chi-square test, and the statistical significance was defined as $p < 0.05$.
Results: A total of 343 patients were enterd during the period. All patients were female and the mean age was 55.9 years old. SN metastasis was detected in 79 cases (23%). The mean tumor size was 18.9 mm (median 16 mm) and the tumor size was significantly lager in SN positive cases compared with SN negatuve cases ($p < 0.001$). Clinical T-stage has also been relataed with SN metastasis ($p < 0.05$). Moreover, SN metastasis was also correlated with lymphatic involvement, venous involvement and histological type, respectively ($p < 0.05$). On the other hand, there was no significant correlation between SN metastasis and nuclear grade, hormone status, Her2 status, or subtype classification.
Conclusion: Our results suggest that some clinicopathological factors such as invasive tumor size, clinical T-stage, lymphatic and venous involvement and histological type are valid for prediction of SN metastasis. However, subtype classification will not be useful for SN metastatis prediction in our series.
Disclosure of Interest: No significant relationships.

P170
SENTINEL NODE AND OCCULT LESION LOCALIZATION: A SINGLE INJECTION TECHNIQUE

J. Rodriguez *. *Breast Unit, Hospital Modelo, La Coruña, Spain*

Goals: To identify non palpable lesions and sentinel node by using a single injection of a radiotracer the same day of the surgery.
Methods: The morning of the surgery an injection is prepared by using 4 mCi of Tc99m-nanocolloide in 0.4 mL of saline. It is divided in to 2 injections of 1–2 mCi en volumen de 0.1–0.2 mL in case a second injection is needed. After 99Tc has been chemically bound to the particles, they could be injected directly into the occult lesion under stereotactic mammographic or ultrasonic control. In the operating room a gamma ray-detecting probe locates the lesion and has proven invaluable in guiding its complete removal. It is effective, easily reproducible and has a short learning curve. For lesions detected ultrasonically, the radiotracer is injected under the guidance of a linear probe attached to a needle biopsy device which is inserted into the breast manually. The needle tip is positioned at the centre of the lesion, as shown by a change of echogenicity at the lesion site. Radiotracer is then injected, followed by an additional minimal quantity of saline to flush the needle and help avoid dispersing the radioactivity. For lesions visible by US and revealed only mammographically, mammographic equipment attached to a computerized stereotactic system is used to guide injection. Lateral and anterior scintigraphic images are taken after few a minutes and five hours later. The lateral image is obtained with the patient prone using a polystyrene block to hold the breast in position and a flexible wire cobalt source to outline the breast contour. The scintigraphic images are assessed for the presence of radioactive contamination. When the hotspot appears as a small well-delimitated area, the patient is referred for surgery.
Results: This injection technique allows the identification of the non palpable lesion as well as the sentinel node.
Conclusion: This method requires a multidisciplinary team consisting of surgeon, pathologist, nuclear medicine physician and radiologist. It allows the surgeon to localise both the non palpable lesion and the sentinel node in the same surgical time. It allows the surgeon to choose the most direct or most convenient surgical access route the lesion. This has aesthetic implications as well as shortening surgery time. The probe can be used at any time during the operation to check lesion position and ensure that the removed specimen completely contains the hot spot centred within non-radioactive active tissue.
Disclosure of Interest: No significant relationships.

P171
OUR NOVEL ENDOSCOPY-HYBRID SURGERY: THE PURSUIT OF COSMETIC IMPROVEMENT AND CURABILITY

H. Tanaka*, M. Kubo, M. Tanaka. *Surgery and Oncology, Kyushu University, Fukuoka City, Fukuoka Pref., Japan*

Goals: We developed novel Endoscopy-Hybrid breast conservation surgery for primary breast cancer by applying endoscopic breast surgery devices (Breast-Retractor, Karl Storz) since 2007. Our indication of this surgery is restricted to T1 cases without extensive intraductal spread. Our goal is to determine the safeness, curability and cosmetic improvement of Endoscopy-Hybrid breast conservation surgery, compared with conventional breast conservation surgery.
Methods: We assessed 290 patients with primary breast cancer who underwent breast conservation surgery (BCS) in our department from September, 2007 to November, 2011. We performed Endoscopy-Hybrid BCS for 84 cases and conventional BCS for 206 cases, combined with sentinel lymph node biopsy or level I axillary dissection carried out under direct vision. We reviewed and weighed operative duration, amount of bleeding and positive surgical margin rate between two groups, and follow up local recurrence and overall survival rate.
Results: In conventional BCS group, median operative duration was 102 minutes, mean amount of bleeding was 35 gram, and positive surgical margin rate was 20.4%. In Endoscopy-Hybrid BCS group, median operative duration was 140 minutes, mean amount of bleeding was 21 gram and positive surgical margin rate was 19.0%. Endoscopy-Hybrid BCS required more operative duration, but the amount of bleeding decreased significantly. Positive surgical margin rates showed no significant differences in both groups. These results (operative duration, bood loss, positive margin rate) also showed no significant differences in each operator (three surgeons in our department), thus, this new procedure considered easy to learn relatively. About the curability, no significant differences of local recurrence and overall survival rates were observed between two groups after a follow-up period of 30 months. For cosmetic improvement, we could perform more extensive skin flap formation and dissection of mammary gland from pectoral major muscle by employing Endoscopy-Hybrid method. As a result, we could achieve more mobilization of breast tissue and appropriate mammoplasty after BCS.
Conclusion: Our Endoscopy-Hybrid BCS can minimize skin incision, reduce blood loss, and improve reconstructive outcome. This technique is also very safe, easy to learn, and well accepted by patients.
Disclosure of Interest: No significant relationships.

P172
IS IMLN DISSECTION NEEDED, WHEN ONLY IMLN METASTASIS SUSPECTED?

J.E. Choi*, Su Hwang Kang, S.J. Lee, G.T. Son, J.H. Lee. *General Surgeon, Yeungnam University College of Medicine, Daegu, South Korea*

Goals: Metastatic status of internal mammary lymph nodes (IMLNs) has a clinical importance in assessing stage and prognosis of breast cancer. But, when metastasis of IMLN is suspected, the management is controversial. We reviewed 37 breast cancer patients who had IMLN dissection, retrospectively, and investigated the pathologic status of IMLNs.
Methods: From August 2005 to December 2011, at Yeungnam University Hospital, 43 patients underwent IMLN biopsy or dissection for suspected IMLN metastasis on lymphoscintigraphy, breast ultrasound or PET CT, when diagnosed with primary or recurred breast cancer. 6 patients who had stage IV at diagnosis or had too obscure data to identify exact location of IMLN, were excluded. Clinicopathologic features of these patients and metastatic status of IMLNs was investigated.
Results: Total 37 patients were included in this study. 25 patients and 12 patients underwent IMLN dissection when diagnosed with primary or recurred breast cancer, respectively. Unlike conventional IMLN dissections, our IMLN biopsy or dissection was done during Radical mastectomy (in 2 pts.), modified radical mastectomy (in 21 pts.), using incision of breast conserving surgery (in 3 pts.) and separated incision (in 11 pts.), with or without resection of ribs. The mean number of IMLNs was 2.5 ± 2.1 and total metastatic rate of IMLN was 62.1% (23/37). On lymphoscintigraphy, ultrasound and PET CT, IMLN metastasis was suspected in 7, 1 and 29 patients. Among them, IMLN metastasis was confirmed on pathologic examination in 2 (28.5%, 2/7), 0 (0%, 0/1) and 21 (72.4%, 21/29) patients, respectively. In PET CT, which method showed the highest detection rate, sensitivity, specificity, positive predictive value, and negative predictive value was following: 91.3%, 42.8%, 72.4% and 27.6%. Mean standard uptake value (SUV) of metastatic and non-metastatic IMLN were 3.6 ± 2.9 and 3.9 ± 2.6 and there was no statistical difference (p-value = 0.821). During IMLN dissection, besides initial approach intercostals space (ICS), some metastatic IMLN was also found in upper or lower level ICS (42.9%, 6/14). Only IMLN metastasis without axillary nodes metastasis were found in 4 patients and the tumor location of these patients was all inner or central quadrant. Chest X-ray was done postoperatively as routine procedure, and there were no other specific complications such as pneumothorax or hemothorax.
Conclusion: IMLN dissection without radical mastectomy can be done safely without complications due to recent advance in diagnostic and surgical skills. If SUV on IMLN is shown on the PET-CT, IMLN dissection is needed, regardless of SUV. If breast cancer is located at inner quadrant, more aggressive dissection of IMLN is needed. Further follow-up and studies are needed to assess locoregional recurrence and to compare improvement in overall survival and disease free survival.
Disclosure of Interest: No significant relationships.

P173
OSNA IS USEFUL BUT COPY NUMBER OF OSNA MIGHT NOT BE A PREDICTIVE OR PROGNOSTIC FACTOR

M. Suzuki*. *Breast Center, Kitamurayama Hospital, Higashine Yamagata, Japan*

Goals: SLN (sentinel Lymph node) biopsy is a common procedure in surgical treatment of clinically node-negative breast cancer patients. OSNA (One-step nucleic acid amplification) is a semi-automated examination using molecular biological technique and allows straightforward diagnosis of SLN metastasis without a pathologist by quantitative evaluation of CK19 m-RNA as a copy number of OSNA. In this study, we compared OSNA analysis to histological investigation by pathologists for determining the suitability of OSNA, and we also examined that the copy number of OSNA is related with IHC4 (ER status, PgR status, HER2 expression and Ki-67 index) of primary tumor. SLN (sentinel Lymph node) biopsy is a common procedure in surgical treatment of clinically node-negative breast cancer patients. OSNA (One-step nucleic acid amplification) is a semi-automated examination using molecular biological technique and allows straightforward diagnosis of SLN metastasis without a pathologist by quantitative evaluation of CK19 m-RNA as a copy number of OSNA. In this study, we compared OSNA analysis to histological investigation by pathologists for determining the suitability of OSNA, and we also examined that the copy number of OSNA is related with IHC4 (ER status, PgR status, HER2 expression and Ki-67 index) of primary tumor.
Methods: Surgically obtained 138 SLNs from 94 breast cancer patients were evaluated and compared. The SLNs were sectioned into three pieces along the major axis. The central piece was sliced into 1 mm wide and sent to pathologists in an outside

laboratory for postoperative histological investigation with H&E and immunohistochemical staining to diagnose metastatic negative or positive. The other two pieces were examined with the OSNA method of counting the copy number to diagnose metastatic negative or positive during an operation. Further more, we compared the copy number of OSNA to IHC4 of the primary tumor.

Results: 130 SLNs were same diagnosis using both methods. 105 SLNs were negative and 25 SLNs were positive using both methods. 4 SLNs were positive on OSNA but negative on histology. Other 4 SLNs were negative on OSNA but positive on histology, and these 4 nodes contained only micrometastasis lesion. The concordance rate was 94.2% and specificity was 96.3%. Our statistic analysis did not show any relationship between the copy number of OSNA and the IHC4.

Conclusion: These results suggest that OSNA is a very useful for detecting SLN metastasis. IHC4 are known as factors of prediction and/or prognosis of breast cancer, but a copy number of OSNA might be an independent factor from prediction and prognosis.

Disclosure of Interest: No significant relationships.

P174
OUTCOME ANALYSIS OF ONCOPLASTIC BREAST SURGERY

J.J. Lee[1] *, H.H. Choi[2], W.W. Kim[1], S.O. Hwang[2], J.H. Jung[2], H.Y. Park[2], Y.H. Lee[1], J.D. Yang[3], S.J. Lee[4]. *[1]Department of Surgery, Kyungpook National University School of Medicine, Daegu, South Korea, [2]Department of Surgery, Kyungpook National University School of Medicine, Daegu, South Korea, [3]Department of Plastic and Reconstructive Surgery, Kyungpook National University School of Medicine, Daegu, South Korea, [4]Department of Oncology and Hematology, Kyungpook National University School of Medicine, Daegu, South Korea*

Goals: Despite the increase of oncoplastic surgery to facilitate breast conservation, discussions regarding the oncological safety are not specifically conducted. The aim of this study was to determine oncological outcome of oncolplastic surgery from a single institution.

Methods: A retrospective analysis was performed on 298 cases underwent oncoplastic breast conserving surgery between Sep. 2006 and Dec. 2010. The histologic diagnosis, tumor size, location, margic status, re-excision, recurrence and breast oncoplastic technique type were analyzed.

Results: The mean age was 50 years (range, 28 to 79 years), with a median follow-up of 45 months (range, 24 to 76 months). Invasive ductal carcinoma was the most common type of breast cancer and the most common location of tumor was upper outer quadrant (41.4%) and the average size of the tumor was 1.52 cm (range, 0.2–3.5 cm). The overall rated of completion mastectomy for positive margins was 1 percent. Tumor size, tumor location and operation procedure were not found to correlate with undergoing re-excision for positive margins. Distant disease-free survival rates were 98.3 percent with local recurrence in 0.4 percent.

Conclusion: Breast conserving treatment with oncoplastic surgery has local recurrence rates and survival rates comparable to standard breast conservation. Oncoplastic surgery has emerged from the increasing trend toward breast conserving treatment and the recognized need to improve the cosmetic outcomes of this approach. The incorporation of oncological and plastic surgery techniques allows for the complete resection of local disease while contributing to improvement in cosmetic outcomes and overall patient satisfaction.

Disclosure of Interest: No significant relationships.

P175
MULTICENTER CROSS-SECTIONAL STUDY COMPARING QUALITY OF LIFE, BODY IMAGE AFTER BREAST CANCER SURGERY

D.J. De Maeseneer[1] *, M. Strijbos[1], P. Blondeel[2], R. Van Den Broecke[3], H. Depypere[3], G. Braems[3], H. Denys[1], S. Van Belle[1], V. Cocquyt[1]. *[1]Medische Oncologie, UZ Gent, Gent, Belgium, [2]Plastische Heelkunde, UZ Gent, Gent, Belgium, [3]Gynecology, UZ Gent, Gent, Belgium*

Goals: Current guidelines propose both breast conserving surgery and mastectomy with or without reconstruction in early breast cancer patients. Although a more conservative surgical approach aims to improve post-operative quality of life, multiple studies have failed to show a clear benefit. This study uses an extensive database of a post-operative quality of life survey in Flanders to discover small but significant differences in quality of life and body image between breast conserving surgery (BCS), mastectomy and mastectomy followed by reconstruction.

Methods: Early breast cancer patients of 8 breast cancer clinics were surveyed in this cross-sectional study. The questionnaires consisted out of the EORTC QLQ-30 (version 3) and EORTC BR-23 validated quality of life questionnaires and a Body Image Scale. Statistical differences in quality of life scores between the three treatment groups (mastectomy without reconstruction, mastectomy with reconstruction and breast conserving surgery) were assessed in univariate analysis and possible associations between scores and patient/treatment characteristics were assessed using quantile regression analysis.

Results: We analyzed data from 655 breast cancer patients. More than half underwent breast-conserving surgery (57.2%), 180 women had mastectomy without reconstruction (27.5%) and 100 women had mastectomy with reconstruction (15.3%). Patients characteristics were significantly different between treatment groups. Global health status showed an advantage for the mastectomy with reconstruction patients but this was not significant (P = 0.066). Body image was significantly better in BCS patients compared to both mastectomy groups, which showed no significantly different scores. Multivariate analysis did show a clear beneficial effect of BCS on global health scores compared to the mastectomy without reconstruction group (P 0.002) but not in comparison with the mastectomy with reconstruction group. Body Image scores stayed in favour of BCS in multivariate analysis.

Conclusion: In our study, mastectomy with reconstruction patients showed the best global health status scores outperforming both breast conserving surgery and mastectomy without reconstruction patients. Differences were not large and not statistically significant in univariate analysis. We confirmed the impact of type of breast cancer surgery on body image. Using validated questionnaires and excluding patients with a short interval after surgery, we found that body image in the breast conserving surgery group was significantly better compared to the two mastectomy groups. There is a small benefit of reconstruction after mastectomy, which was not significant. In early breast cancer, pre-operative multidisciplinary counselling seems necessary, explaining possible implications of each surgical treatment choice.

Disclosure of Interest: No significant relationships.

P176
THE SAFETY, SURGICAL INVASION, AND COSMETIC APPEARANCE OF ENDOSCOPIC BREAST-CONSERVING SURGERY

H. Takahashi *, T. Fujii, Y. Inoue, S. Nakagawa. *Breast Care Center, Kyusyu medical center, Fukuoka, Japan*

Goals: Breast-conserving surgery for breast cancer is a surgical procedure that causes significant changes to the postoperative cosmetic appearance of the breast, such as breast deformation, concavity, and keloid formation in the wound. Endoscopic breast surgery has been used in many cases to achieve a favorable cosmetic

appearance without leading to inferior curative outcomes for breast cancer compared with conventional surgical procedures (surgery under direct vision). We investigated the usefulness of endoscopic surgery by comparing it with surgery under direct vision.

Methods: For this, we compared the safety, extent of surgical invasion, and cosmetic appearance of 100 patients who underwent endoscopic surgery at our hospital and 150 patients who underwent surgery under direct vision during the same period. Eligible patients were given an explanation of both surgical procedures, and the patients then selected the procedure they would undergo. Safety was assessed by measuring intraoperative hemorrhage volume, operation duration, and the presence or absence of complications. The extent of surgical invasiveness was assessed through pre- and postoperative measurements of inflammatory cytokine IL-6 and other parameters. Cosmetic appearance was assessed using a patient satisfaction survey conducted postoperatively, while patients were being followed up on an outpatient basis.

Results: While there was no significant difference between the groups in terms of hemorrhage volume (P = 0.6784) or any serious postoperative complications, operation duration in the endoscopic surgery group was prolonged by 19 min on average compared with the direct vision surgery group (P < 0.001). No significant differences in the extent of surgical invasiveness were noted between pre- and postoperative leukocyte counts, neutrophil counts, or IL-6 levels. When the cosmetic appearance was compared using pre- and postoperative photographs, concavity in the operative wound and removal site was found to be markedly less noticeable after endoscopic surgery than after surgery under direct vision. In the patient satisfaction survey, conducted while patients were being followed up on an outpatient basis after surgery, the endoscopic surgery group indicated significantly high satisfaction with regard to the items wound conditions (P = 0.0064), concavity (P = 0.01), and breast shape (P = 0.041). Furthermore, as of October 2012, no cases of local recurrence have been noted in either group.

Conclusion: While the present study did not reveal any differences between endoscopic surgery and direct vision surgery in terms of safety or the extent of surgical invasiveness, the postoperative satisfaction survey revealed higher satisfaction for cosmetic appearance in the endoscopic surgery group than in the direct vision group. Therefore, we were able to conclude that this procedure is useful for the management of breast cancer.

Disclosure of Interest: No significant relationships.

P177

PROGNOSTIC COMPARISON OF CONSERVING BREAST SURGERY BETWEEN TNBC AND NON-TNBC

D. Wu*, Z. Fan. *Breast Surgery, First Hospital of Jilin University, Changchun, China*

Goals: To investigate the prognostic difference of breast conservative surgery between triple negative breast cancer (TNBC) and non-triple negative breast cancer (non-TNBC).

Methods: 2151 patients were diagnosed with breast cancer and performed surgery in the First Hospital of Jilin University from 2002 to 2010. Among them, 265 patients (12.3%) recieved breast conservative surgery. 50 patients were TNBC and 215 patients were non-TNBC. Follow-up deadline for July 30, 2012. Locoregional recurrence-free survival (LRRFS), distant metastasis-free survival (DMFS), and overall survival (OS) were measured from the date of definitive surgery to the date of the first documented LRR, distant metastasis, or death, respectively; Kaplan–Meier method was used to calculate the survival rate and draw the survival curve. Log-rank test was applied to compare the difference between the survival curves. P-values of <0.05 were considered statistically significant. Statistical analyses were carried out by Spss software, version 18.0.

Results: Age, tumor size, lymph node status, cancer stage and postoperative treatment between the two groups were no differences (p > 0.05). Follow-up rate was 95.5%. The median follow-up among all patients was 37 months (range 7–119 months). Most patients recieved radiotherapy. Twelve patients refused to recieve radiotherapy. The 1-, 3- and 5-year OS rate of TNBC was 98.0%, 94.6%, 69.4%, repectively, lower than non-TNBC (99.0%, 96.9%, 93.4%, repectively, p = 0.032). The 1-, 3- and 5-year LRRFS rate of TNBC was 100%, 100%, 100%, repectively, without signifinant difference with non-TNBC (100%, 98.5%, 97.5%, respectively, p = 0.534). The 1-, 3- and 5-year DMFS rate of TNBC was 97.7%, 89.4%, 74.5%, repectively, without statistically signifinant difference with non-TNBC (98.1%, 94.8%, 89.8%, respectively, p = 0.283).

Conclusion: For conserving breast surgery, OS of TNBC was poorer than non-TNBC. But local recurrence rate of TNBC was not higher than non-TNBC perhaps because almost all petients who were performed conserving breast surgery recieved radiotherapy.

Disclosure of Interest: No significant relationships.

P178

OUR INITIAL EXPERIENCE OF ONCOPLASTIC BREAST CONSERVATION SURGERY

S. Khawaja*, A.M. Huws, K. Nadi, I. Patchell, S. Khaliq, G. Dazeley, A. Barnett, Y. Sharaiha, S.D. Holt. *Department of Surgery, Prince Philip Hospital, Llanelli, United Kingdom*

Goals: Our institution has recently implemented oncoplastic techniques for breast conservation. Our aims were: 1. To provide patients with breast conservation and cosmesis. 2. To decrease the rate of mastectomy.

Methods: Patients were chosen prospectively. The procedures were indicated in those who would have more than 10–15% of the breast volume excised at the time of the surgical intervention. They were also indicated in tumors in unfavorable sites of the breast, specifically the inner quadrants. The surgical procedures which were applied were primarily volume displacement techniques. These included horizontal rotational flaps for inner quadrant tumors; vertical rotational flaps for lower quadrant tumors; the shutter technique for upper outer quadrant tumors; the Grisotti technique for central tumors; and intramammary flaps for small tumors. They were not performed in patients requiring a mastectomy. These latter patients had multicentric disease and widespread microcalcifications representing diffuse DCIS.

Results: A total of 21 patients were operated with the new surgical methods from September 2011 to November 2012. These included 8 shutter techniques; 6 vertical rotational flaps; 4 horizontal rotational flaps; 2 intramammary flaps; and 1 grissoti flap. The age of the patients ranged from 44 to 77 years with a mean of 52 years. The histology of the tumors were 14 infiltrating ductal carcinomas; 3 infiltrating lobular carcinomas and 3 patients with DCIS. 3 tumors were grade I; 11 were grade II; and 3 were grade III. Only 2 tumors were ER negative. The size of the tumors were 10 mm to 75 mm with a mean of 32 mm. 14 had negative margins ranging from 1 mm to 15 mm (5.56 mm). 7 patients had positive margins which were defined as the tumor involving the margins. Out of these patients, 5 underwent completion mastectomies and 2 underwent a wider excision with no residual disease in the final histology. Out of the patients who had positive margins, none had lymphovascular invasion. The type of cancer in these patients were 3 infiltrating ductal carcinomas; 2 infiltrating lobular carcinomas; and 2 cases of DCIS. The two patients with extensive disease (41 mm and >50 mm), only 1 was predicted preoperatively. Out of the 2 with multifocal disease, only 1 was correctly detected preoperatively. Only 2 patients had delayed wound healing. These were the ones who had horizontal rotational flaps. This did not effect their adjuvant treatment, though they did have multiple visitis to the clinic.

Conclusion: In cases of infiltrating lobular carcinomas, rotational flaps should be considered due to unfavorable positions rathar than the extent and multifocality. Clips must be placed not only in the

cavity but along the approximated margins. To avoid prolonged wound healing in horizontal rotational flaps, a closure must be performed in two layers. The oncoplastic techniques do allow wider margin excisions of tumors.

Disclosure of Interest: No significant relationships.

P179

PREDICTING THE PRESENCE OF NON SENTINEL LYMPH NODE METASTASES IN EARLY BREAST CANCER PATIENTS

W.S. Yong[1] *, K.M. Chue[1], A.A. Thike[2], S.S. Ahmed[2], H.H. Li[2], P.H. Tan[2]. *[1]Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore, [2]Singapore General Hospital, Singapore, Singapore*

Goals: To determine the validity of the Memorial Sloan-Kettering Cancer Centre (MSKCC) breast cancer nomogram for predicting the likelihood of additional non-sentinel lymph node (SLN) metastases in patients with a positive SLN biopsy, in the Singaporean breast cancer population, and to identify important clinicopathologic parameters that are most helpful in predicting non-SLN metastasis.

Methods: We reviewed over a thousand patients undergoing SLN biopsy from July 2004 to October 2009. A total of 266 patients were identified who had primary invasive breast cancer and a positive SLN biopsy for which axillary clearance was done. The MSKCC nomogram was applied to these patients, and it's predictive value was determined by calculating the area under the curve (AUC) for the receiver-operator characteristics (ROC) curve. A bootstrapped simulated population of 200 patients were then used to subsequently create our own Singapore General Hospital (SGH) nomogram.

Results: The MSKCC nomogram achieved an AUC of 0.716 (range 0.653–0.779) in our study population, while the SGH nomogram, which utilised only 3 clinicopathologic parameters namely lymphovascular invasion, number of positive and negative sentinel lymph nodes biopsied, achieved an AUC of 0.750 (range 0.691–0.808).

Conclusion: The MSKCC nomogram is validated in the SGH patient population. The SGH nomogram shows promise to be equally, if not, more predictive as a model in our own population, while utilising only 3 clinicopathologic parameters. We would need to prospectively validate our SGH nomogram.

Disclosure of Interest: No significant relationships.

P180

FREE DERMAL FAT GRAFT FOR BREAST RECONSTRUCTION WITH SIMULTANEOUS BREAST-CONSERVING SURGERY

T. Ohno[1] *, K. Inoue[1], H. Tokai[1], S. Nagayoshi[1], A. Yoneda[1], S. Ohno[1], M. Morita[1], T. Fukuda[2], J. Irie[3], Y. Tokai[4]. *[1]Surgery, Nagasaki Municipal Hospital, Nagasaki, Japan, [2]Radiology, Nagasaki Municipal Hospital, Nagasaki, Japan, [3]Pathology, Nagasaki Municipal Hospital, Nagasaki, Japan, [4]Surgery, Imamura Hospital, Nagasaki, Japan*

Goals: The aim of this study was to summarize our experiences with seven cases of simultaneous breast-conserving surgery and breast reconstruction using a free dermal fat graft (FDFG) for early breast cancer.

Methods: Between June 2011 and September 2012, 54 consecutive female patients with breast cancer were admitted to our hospital. Among them, seven patients underwent breast conserving surgery (BCS) with FDFG reconstruction. FDFG was indicated for patients who satisfied the following criteria: primary breast cancer located at the B, D, E area, for which it can be difficult to maintain good cosmesis after BCS; early breast cancer such as N0, no ly infiltration and no invasion to the skin or muscularis; and free from positive surgical margins. The procedures, including both BCS and sentinel node biopsy, were performed under general anesthesia, and the surgical margin of the breast and node-negative status were both pathologically confirmed using frozen sections. Afterwards, as part of the FDFG procedure, we marked the location of the free fat graft on the patient's lower abdominal skin. Next, the epidermis was shaved using a knife, and the fat graft was removed with the dermis from the lower abdomen. The free dermal fat graft was then transferred to the defect of the breast-resected site, from the dermis side at the muscular side. The clinicopathological characteristics were evaluated, as were the results of the FDFG reconstruction.

Results: The mean age of the seven patients was 52.3 years (range 43–63 years). The main location of the primary breast cancer was the B area of five patients and the CE area of two patients. The mean diameter of the tumor was 19.6±18.8 mm (range 5–60 mm). Six of the patients were node negative, and one case with positive lymph nodes was revealed in HE section. All surgical margins were free. The pathological diagnosis was one case of DCIS, four cases of scirrhous carcinoma, one case of solid tubular carcinoma, and one atypical proliferative lesion. Five cases were ER positive and two were HER2 positive. With regard to the surgical procedure, all cases underwent breast conserving surgery and sentinel lymph node biopsy. The mean size of the resected specimen of the breast was 47.8±16.1 cm^2 (range 35–72 cm^2). All fat grafts were harvested from the lower abdominal wall, and the mean graft size was 63.2±32.3 cm^2 (range 35–120 cm^2). The total length of the operation was 222.6±50.9 min (range 155–321 min), and the blood loss was 19.3±13.4 mL (range 0–30 mL). None of the grafts developed necrosis or a wound infection, and the mean hospital stay was 8.9 days (range 6–12 days). The patients' cosmetic results were fair without any deformity, but there were five cases of rigidity and one patient developed and oil cyst. There was no recurrence and no mortality.

Conclusion: Simultaneous breast reconstruction using a FDFG was feasible and useful for early breast cancer patients undergoing breast conserving surgery.

Disclosure of Interest: No significant relationships.

P181

CT-LYMPHOGRAPHY-GUIDED SENTINEL NODE BIOPSY AND THE DETECTION OF METASTASES IN BREAST CANCER

K. Motomura[1] *, H. Takahashi[1], T. Nakayama[1], Y. Tamaki[1], K. Nakanishi[2]. *[1]Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan, [2]Radiology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan*

Goals: We previously demonstrated that CT-lymphography (CT-LG) can distinguish true sentinel nodes (SNs) from non-SNs, and that true SNs can be used for accurate staging of the axilla in patients with breast cancer (SABCS 2010). In this study, the detection of nodal metastases using CT-LG-guided SN biopsy (SNB) was compared with that by standard SNB without CT-LG in patients with breast cancer.

Methods: Between February 2008 and September 2010, 175 patients underwent CT-LG-guided SNB and 353 patients underwent standard SNB. Contrast agent was injected intradermally into the skin overlying the breast tumor and in the subareolar region in CT-LG. The marking of the location of the true SN was performed on the skin surface using a CT laser light navigator system. SNB was performed using a combination of dye and radioisotope. Lymph nodes located just under the marking were removed as true SN in the CT-LG group. All dyed nodes or all hot nodes were removed as SN in the standard group.

Results: The SN identification rates were 100% for the CT-LG group and 98.3% for the standard group, and there was no significant difference between them ($p = 0.185$). In the CT-LG group, fewer SNs per patient were identified than in the standard group (1.1 vs 1.6, $p < 0.0001$). The detection rate of nodal metastases was similar between these two approaches on a patient basis (25.1% vs 22.2%, $p = 0.443$), but was higher in the CT-LG group on a nodal basis (24.3% vs 16.4%, $p = 0.015$).

Conclusion: The use of CT-LG-guided SNB was associated with fewer SNs and a higher detection rate of nodal metastases on a nodal basis compared with standard SNB.

Disclosure of Interest: No significant relationships.

P182

LOCOREGIONAL RECURRENCE AFTER CONSERVATIVE SURGERY FOR DUCTAL BREAST CANCER: ROLE OF SURGICAL MARGIN

E. Botteri[1]*, V. Lohsiriwat[2], G. Curigliano[3], N. Rotmensz[1], P. Veronesi[4], M. Casales Schorr[2], G. Renne[5], M.G. Mastropasqua[5], B. Santillo[1], R. Orecchia[6], G. Viale[7], M. Rietjens[2], A. Goldhirsch[3].
[1]Division of Epidemiology and Biostatistics, European Institute of Oncology, Milano, Italy, [2]Division of Plastic Surgery, European Institute of Oncology, Milano, Italy, [3]Division of Medical Oncology, European Institute of Oncology, Division of Medical Oncology, Milano, Italy, [4]Department of Breast Surgery, European Institute of Oncology, Milano, Italy, [5]Department of Pathology, European Institute of Oncology, Milano, Italy, [6]Department of Radiation Therapy, European Institute of Oncology, Milano, Milano, Italy, [7]Division of Pathology, European Institute of Oncology, Milano, Italy

Goals: Minimizing tumor recurrence in the breast is of major clinical importance, since local recurrence may be associated with reduced survival and emotional distress. We evaluated the role of surgical margin on the risk of locoregional recurrence in a large retrospective mono-institutional series of women with breast cancer.

Methods: We analyzed data from 5,151 consecutive patients with primary invasive ductal breast cancer who underwent quadrantectomy and external radiotherapy at the European Institute of Oncology in Milan, Italy, from January 2000 to March 2009. Margin status was classified in four categories, according to the smallest distance from surgical margins to invasive or ductal in situ neoplasia: (a) 0 mm (i.e. positive margins), (b) >0 mm and <1 mm, (c) ≥1 mm and <10 mm and (d) ≥10 mm.

Results: Median age was 52 years and median tumor size was 1.5 cm; 2,995 (58.1%) women had a node negative disease. Margin status distribution was as follows: positive margins in 110 (2.1%) cases, >0 and <1 mm in 363 (7.1%), ≥1 and <10 mm in 392 (7.6%) and ≥10 mm in 4,286 (83.2%). After a median follow-up of 80 months, we observed 201 locoregional first events and 376 deaths, corresponding to 10-year cumulative incidences of 5.9% and 11.4%. After adjusting for age, tumor size, lymph nodal involvement, perivascular invasion, multifocality, extensive in situ component and molecular subtype, margin status was significantly associated with the risk of locoregional recurrence: taking ≥10 mm as reference category, hazard ratios (HRs) with 95% confidence intervals (CIs) were 2.33 (1.18; 4.19) for positive margins, 1.82 (1.20; 2.76) for >0 and <1 mm and 1.67 (1.04; 2.69) for ≥1 and <10 mm. The effect of margins on locoregional recurrence risk significantly decreased as the age of the patients increased (P for interaction: 0.011). Margin status had no statistically significant impact on overall survival (HR 0.99 (95% CI 0.75–1.31) for <10 mm vs >10 mm).

Conclusion: Patients with positive margins as well as those with a clearance of tumor at the surgical margin <10 mm had a higher risk of locoregional recurrence compared to patients with wider cancer-free surgical margins (≥10 mm). However, margin status had no impact on overall survival.

Disclosure of Interest: No significant relationships.

P183

PROGNOSIS OF EARLY BREAST CANCER PATIENTS TREATED WITH RADIOFREQUENCY ABLATION

K. Miyamoto*, S. Imoto, H. Isaka, H. Ito, K. Imi, M. Kitamura. *Breast Surgery, Kyorin University School of Medicine, Mitaka, Japan*

Goals: After a phase I study on radiofrequency ablation (RFA) followed by immediate partial mastectomy (Breast, 18: 130–4, 2009), we started a phase II study of RFA alone in 2009.

Methods: T1 and sentinel node-negative breast cancer patients who had no extensive intraductal components were enrolled. Primary endpoint was breast deformity after RFA and secondary endpoints were ipsilateral breast tumor recurrence and quality of life examined with FACT-B. RFA was performed using a LeVeen electrode and an RF-2000 generator (Boston Scientific Corporation, USA) following Izzo's protocol (Cancer, 92: 2036–44, 2001). Breast deformity and breast imaging were recorded at 3, 6 and 12 months after RFA.

Results: As of September 2012, 19 of the 22 eligible patients agreed to undergo RFA. There were no severe adverse events in all patients except pain relief with NSAID for a few days. Most patients received adjuvant hormonal therapy and breast irradiation. MR mammography showed degenerative change with ring enhancement that was consistent with red ring observed in the margin of ablated breast specimen at phase I study. All patients have been disease-free at the median follow-up of 27 months (range: 5–41 months).

Conclusion: Indication of RFA in breast cancer is strictly limited for early stage patients, but RFA is a promising local treatment as an alternative to partial mastectomy.

Disclosure of Interest: No significant relationships.

P184

USE OF INTRAOPERATIVE ULTRASOUND IN THE ASSESSMENT OF MARGINS IN BREAST CONSERVING SURGERY

W.P. Lee[1]*, S.K. Lim[1], C.W. Mok[2], C. Seah[2], J. Seah[2], S.M. Tan[2].
[1]General Surgery, Changi General Hospital, Singapore, Singapore, [2]Changi General Hospital, Singapore, Singapore

Goals: In this study, we aim to assess the correlation of intraoperative ultrasound (IOUS) margins with histological margins in breast conserving surgery, as well as find possible confounders which may influence the accuracy of the IOUS. We also compare the re-excision rates between patients who underwent palpation guided surgery with those who had IOUS performed in our centre.

Methods: A retrospective review of a prospectively collected database yielded 86 patients who had undergone breast conserving surgery at our centre from December 2004 to March 2012. The excised specimen was examined intra-operatively with the aid of ultrasound to ensure a minimum margin of 15 mm. The margins were assessed histologically and correlated with the IOUS findings. Re-excision was offered when the pathological margins was <10 mm.

Results: 86 patients with 87 tumours were included and hence, we yielded a total of 384 margins for analysis. There was good correlation between the margins recorded by ultrasound and pathological margins ($r = 0.564$ $p < 0.001$). We also demonstrated that, with a minimum IOUS margin of 15 mm, 94.9% of our patients were able to secure a minimum histological margin of 2 mm. 39 of the 86 patients (45.3%) had margins re-excised at the time of surgery when the IOUS margins were found to be less than 15 mm and of these, only 8 patients (22.2%) had to undergo second operation for involved margins. Comparing with the group undergoing palpation guided surgery, there were significantly fewer patients who had to undergo a repeat surgery (38.2% vs 9.2%) ($p < 0.001$). The presence of ductal carcinoma-in-situ and tumour size are significant confounders which may influence the accuracy of IOUS in the prediction of pathological margins.

Conclusion: Achieving adequate oncological margins in breast conserving surgery has always been a challenge for breast surgeons. With our data, we conclude that IOUS correlates significantly with histological margins. With the utilisation of IOUS, surgeons are more likely to achieve the desired histological margins, hence significantly reducing the re-excision rates in breast conserving surgery.

Disclosure of Interest: No significant relationships.

P185

THE ANALYSIS OF THE LOCAL TREATMENT OF OUR INSTITUTION BASED ON THE ACOSOG Z0011 TRIAL

A. Horio*, T. Fujita, M. Sawaki, M. Hattori, N. Kondo, A. Ushio, N. Gondo, M. Ichikawa, A. Idota, H. Iwata. *Breast Oncology, Aichi Cancer Hospital, Aichi Nagoya, Japan*

Goals: The clinical trial have suggested no survival benefit for axillary node dissection (ALND) after sentinel lymph node biopsy (SLNB)

in selected patients with clinically node-negative breast cancer who undergo breast conservation therapy (BCT) with whole breast irradiation (WBI) and appropriate systemic therapy. Therefore it can be argued that a change is necessary for breast cancer local treatment in Japan. We compared the results of Z0011 ALND group with the results of the corresponding group at our instituion.

Methods: We identified 85 patients with T1 or T2, clinically N0 breast cancer treated with BCT, ALND after 1 or 2 positive SLNs, and WBI from our database of patients who underwent surgery between April 2002 and December 2010. Date of Lymph nodes, Locoregional DFS, DFS, and OS were compared with those of Z0011 trial.

Results: The median number of nodes removed was 18. Micrometastases identified in SLNs were only 12.9% (less than 37.5% in Z0011 ALND group). At a median follow up of 4.6 years, DFS was 82.3%, Locoregional DFS was 94.1%. (DFS and Locoregional DFS were similar to Z0011 ALND group). There was no axillary lymph node recurrence. Overall survival was 97.6% (better than 91.8% in Z0011 ALND group).

Conclusion: Though the patients in our institution with less micrometastases had higher axillary tumor burden, DFS and Locoregional DFS was equivalent and OS was better than in Z0011. We should not change clinical practice immediately, without considering differences between the Japanese present practice and Z0011 trial well.

Disclosure of Interest: No significant relationships.

P186
IMPACT OF MACROSCOPIC PATHOLOGIC CONTROL ON REEXCISION RATE DURING BREAST CANCER SURGERY

R. Bukovacz[1] *, Z. Csapo[1], L. Vass[2], I. Horvath[2], E. Roman[2], M. Adame[3]. *[1]Surgery, Flor F. County Hospital, Kistarcsa, Hungary, [2]Pathology, Flor F. County Hospital, Kistarcsa, Hungary, [3]Radiology, Flor F. County Hospital, Kistarcsa, Hungary*

Goals: Reduce reexcision rate of breast cancer surgery.

Methods: Surgical margin status is the most significant determinant of local recurrence rate in patients underwent breast conserving surgical therapy. Rexcision rates following surgery vary widely, ranging from 2–50%. In our institute intraoperative macroscopic pathologic measurement of excised mammary sector focusing on free surgical margin is a routine procedure.

Results: Between december 2010 and november 2012 (2 years) we performed 185 breast conserving operations because of breast cancer. Intraoperative macroscopic pathologic measurement proved that surgical margin was 0–2 mm in 7 /3.7%/, 2–5 mm in 45 /24%/, 5–10 mm in 26 /14%/ cases. All of these 78 /42%/ cases we performed an immediate "reexcision". In this two years period there were no need to perform a "real" reexcision (2nd surgery).

Conclusion: Intraoperative macroscopic pathologic control prevents further surgical intervention because of close surgical margin during breast cancer surgery.

Disclosure of Interest: No significant relationships.

P187
Abstract withdrawn

P188
THE EVALUATION OF SKIN INCISION OF MASTECTOMY WITH IMMEDIATE RECONSTRUCTION FOR BREAST CANCER

Y. Hayashi *, T. Shien, S. Watanabe, T. Mizoo, T. Nogami, T. Motoki, N. Taira, J. Matsuoka, K. Kimata, H. Doihara. *Breast Cancer Treatment Reconstruction Center, Okayama University Hospital, Okayama, Japan*

Goals: Although immediate reconstruction of breast has become common surgery for primary breast cancer (BC) patients, there are no definite criteria for its skin incisions. In Okayama University Hospital, breast surgeon and plastic surgeon found a Breast Cancer Treatment and Reconstruction Center (BCTR), and we have discuss and decided about the suitable operative methods including skin incisions in each case. The Goal of this research is to compare an esthetic outcome and curability among each skin incisions and to discuss their validity.

Patients and Methods: We retrospectively reviewed 104 patients who underwent breast surgery for primary BC with immediate breast reconstruction between 2007 and 2011 at BCTR to evaluate a cosmetic outcome and curability among each skin incisions [antero-axial (AA), Stewart's transverse (ST), periareolar (P) and inflamammatory incision (IM)]. We evaluated the cosmetic outcome (size, skin and nipple color, shape, scar, nipple position, breast height) according to Yano's score (Annals of Plastic Surgery 2008), local recurrence rate and clinicopathological feature.

Results: The mean age was 46 (range: 24–65). Clinical T stage was Tis: 27 (22%), T1: 19 (18%), T2: 38 (35%), T3: 14 (13%), T4: 6 (6%). Neoadjuvant chemotherapy was performed on advanced cancer patients: 29 (28%). Reconstruction methods were latissimus dorsi flaps (LD): 52 (52%), DIEP flap: 29 (28%), Tissue expander: 23 (22%). Skin incisions were AA incision: 50 (48%), ST incision: 30 (28%), P incision: 14 (13%), IM incision: 3 (3%). The median Yano's score of AA, ST, P and IM were 6.6, 4.4, 5 and 7 for all patients and 6.9, 5, 6.4 and 7 for the patients who were removed nipple respectively. AA was significantly better score than TS ($p < 0.01$). Operation time of P was relatively one hour longer than that of other incisions. Only 1 patient had a local skin recurrence, and she was performed P incision. The patients with locally advanced BC relatively underwent operation with ST.

	No of pts.	Yano's score (median)	p-value	Median Op time
AA	50 (48%)	6.6		195
ST	30 (28%)	4.4	<0.001	200
P	14 (13%)	5	N.S.	274
IM	3 (3%)	7	N.S.	185
Total	104	5.6		201

Conclusion: AA incision had better cosmetic outcomes than others according to Yano's scoring evaluation. Local recurrence rate was few, but preoperative estimation of skin incision appropriated for tumor size and location is important.

Disclosure of Interest: No significant relationships.

P189
AN EVALUATION OF ELIGIBILITY AND UTILISATION OF BREAST CONSERVATION TREATMENT IN AN ASIAN COMMUNITY

M.P. Tan *, A.S. Sim. *Breast Surgical Oncology, MammoCare The Breast Clinic & Surgery, Singapore, Singapore*

Goals: The objective of this study was to evaluate breast conservation treatment (BCT) rates in an Asian context and to compare them with reported data to assess if utilisation of BCT is optimised.

Methods: All patients who underwent breast conservation treatment (BCT) at a private surgical facility between 2009 and 2011 were included in the study. Patients were deemed to have successful BCT if they underwent breast conserving surgery with clear margins of more than 2 mm and completed all recommended adjuvant treatment.

Results: A total of 166 patients underwent treatment during the study period. The median age was 48. One hundred and twenty-one (72.8%) of the patients had palpable tumours while 45 lesions were screen detected. The tumour sizes ranged from 0.4 to 9.5 cm at the largest dimension. At diagnosis, 20 (12%) had DCIS only, 77 (46.2%) had Stage I disease, 55 (33.1) had Stage II, 12 (7.2%) had Stage III and 1 (0.6%) had metastatic disease. Of 166 patients, 142 (85.5%) women underwent successful BCT. Of these 142, 99 had palpable tumours

and 43 had screen detected lesions. The percentage of women who had symptomatic tumours with successful BCT was 81.8%, while 95.5% of women with image-detected lesions underwent BCT. Twenty-four (14.5%) patients underwent a mastectomy. Of these, 15 (9%) were based on the clinician's recommendations while 9 patients elected for mastectomy despite being advised of the feasibility of BCT. If all patients for whom conserving surgery was recommended underwent successful conservation procedures, then 90.9% of patients would have completed BCT. This would be consistent with the expected rates of BCT that were reported by Scarth. Table 1 compares the results of the current study with that of other published series.

Table 1

Author	n	Patient characteristics	% BCT
Scarth	Guideline estimates		
		Symptomatic	80%
		Screen detected	Abt 100%
Chuwa	767	Symptomatic	28.2%
	(total)	Screen detected	45.2%
Narendra	168	All	52%
McGuire	5865	All	56–67%
Lee		All	63%
Current study	121	Symptomatic	81.8%
	45	Screen detected	95.5%
	166	All	85.5%

Discussion: Mastectomy and BCT offer similar survival outcomes for appropriately selected women with breast cancer. It has been reported that BCT results in improved quality of life with regards to less disruptive body image[7] and lower surgical morbidity. In addition BCT may allow for optimum surgical resource utilisation. It is therefore the authors' opinion that BCT should be the treatment of choice if there are no contraindications.
Conclusion: 85.5% of patients in this study cohort underwent successful BCT. Potentially, a further 5.4% of patients might have undergone successful BCT. Most other series report lower BCT rates than those reported in the current study. Based on the results of the current study, there may be room for a potential increase in utilisation of BCT through patient education, multidisciplinary co-ordination and surgical technique modifications.
Disclosure of Interest: No significant relationships.

P190

THE ROLE OF REAL-TIME VIRTUAL SONOGRAPHY (RVS) IN THE SURGICAL MANAGEMENT OF BREAST CANCER

M. Yoshida*, S. Nakano, K. Fujii, J. Kousaka, Y. Mouri, R. Tetsuka, T. Ando, T. Fukutomi. *Breast and Endocrine Surgery, Aichi Medical University, Aichi, Japan*

Goals: Real-time Virtual Sonography (RVS), which is a newly developed modality, synchronizes sonographic images and MRI-MPR images of the same section in real time. In our previous report, we showed that second-look ultrasonography (US) with RVS system improved the rate of detection of additional MRI lesions that are detectable by MRI but not by conventional imaging. The aim of this study was to evaluate the role of RVS as a supplementary imaging modality in the surgical management of primary breast cancer.
Methods: On the basis of conventional assessment, 81 women with pathology-proven breast cancer were identified as candidates for breast-conserving surgery (BCS) between January 2011 and October 2012. Unless contraindications were present, all of them underwent an ordinary bilateral breast MRI in a prone position. For patients with the additional MRI lesions, we performed second-look US. When we were not able to detect the additional MRI lesions by second-look US, we performed a unilateral breast MRI with the patient in a supine position using a flexible body surface coil and second-look US with RVS which enables the synchronization with supine MR images. The additional MRI lesions that were detectable by second-look US/RVS, if necessary, were confirmed preoperative pathological diagnosis by image-guided needle biopsy. Finally, from pathological examination of the resected specimens, we verified the accuracy of preoperative assessment of tumor extent by the combined use of conventional imaging modality, MRI and RVS.
Results: Out of a total of 78 women; 45 additional MRI lesions were detected (ipsilateral: contralateral = 41: 4). With conventional second-look US, the detection rate for the additional MRI lesions was 42% (19/45), while the rate went up to 87% (39/45) when using RVS. Of the 41additional ipsilateral lesions, 33 lesions in the 33 breasts were suspected malignancy from second-look US/RVS findings and/or preoperative pathological diagnoses and we made changes to the extent of resection (BCS with wider margins than anticipated: Mastectomy = 16: 17): 30 lesions were diagnosed as malignant, while three lesions as benign from the resected specimens. For one woman with an additional contralateral lesion that was preoperatively diagnosed as malignant, we also performed an additional contralateral breast surgery. As a result, the rate of positive margins (the presence of tumor cells within 5 mm of the edge of the resection) after BCS was 18% (11/60). Most of the positive margin cases were incomplete resection of non-invasive disease [17% (10/60)].
Conclusion: RVS made it possible for us to determine the extent of resection for breast cancer more precisely and easily. Our results suggest that using preoperative MRI and RVS in combination with conventional imaging modalities can reduce the rate of incomplete resection of invasive diseases after BCS for breast cancer.
Disclosure of Interest: No significant relationships.

P191

BREAST CANCER IN ELDERLY PATIENTS: OUR EXPERIENCE

P. Grigoropoulos*, M. Danielis, I. Papapanagiotou, V. Kalles, C. Tsikkinis, S. Ammari, A. Gounaris, A. Nisiotis. *1st Surgical Ward, Agii Anargyroi General and Oncological Hospital, Nea Makri, Greece*

Goals: The number of elderly breast cancer patients in the Western world as well as in Greece, has increased in the latest years. In particular the population of the USA ages women over the age of 65 have become a prominent cohort in the breast cancer population, with approximately 50% of all new breast cancers occurring in women aged 65 years and older. The aim of our study was to analyze the characteristics as well as the results of treatment of elderly patients with breast cancer in our unit.
Methods: This retrospective comparative study include 112 patients with breast cancer treated in our surgical clinic during the year 2011. From this patients 46 were aged above 65 years. The following parameters were evaluate: tumor size, histology of tumor, number of lymph nodes with metastases, receptor to estrogen (ER), progesterone (PR) and HER2/neu, type of surgery, surgery at axilla, sentinel node biopsy, margins of excision, surgery re-excisions, postoperative complications, radiation therapy, chemotherapy. Patients divided into two groups, patients aged up to 65 years (group 1) and patients aged over 65 years (group 2).
Results: The median age was 61.8 years (range 38–88). Patients aged up to 65 years (group 1) is a 58.93% and patients aged over 65 years (group 2) is a 41.7% of the population studied. In group 2 (aged >65 years) the average size of the tumor was larger as compared to that in group 1. The histological type of the tumors was similar in both groups. Conservative surgery was performed in 65.75% of patients in group 1 vs 34.3% in group 2 and re-excision was necessary in 4.5% of patients in group 1 vs 2.1% in group 2 because of affected margins. The percentage of the patients with the affected axillary lymph nodes was 32.3% in group 1 and 53.8% in group 2. The ER and PR expression pattern was the following one: ER+ PR+ in 53.9% and 60.8%, ER− PR− in 23.68% and 15.2%, ER+ PR− in 17.1% and 23.9%, ER− PR+ in 5.26% and 0% in group 1 and group 2 respectively.

The overexpression of HER2/new was detected in 38.1% and 51.8% patients in group 1 and group 2. The frequency of complication postsurgery was low but most common in patients in group 2.
Conclusion: In our experience the histological and clinical characteristics were less favourable for elderly patients. For these patients is more common to have increased size of tumors and increased percentage of ER and PR positive tumors and HER2/new overexpression and major axillary involvement. Elderly women are less likely to be offered or received breast conservation surgery.
Disclosure of Interest: No significant relationships.

P192
LONG TERM FOLLOW UP RESULTS ABOUT LOCO-REGIONAL RECURRENCE OF ENDOSCOPIC BREAST CANCER SURGERY
H. Shin*. *Breast and Thyroid Cancer, Myongji hospital, Goyang, South Korea*

Goals: We prefer to endoscopy-assisted breast conserving surgery (BCS) and nipple areolar complex (NAC) preserving mastectomy than conventional breast conserving surgery and mastectomy except T4 stage, older age than 70, inflammatory breast cancer, nipple invasion. Our hospital used to endoscopy for cosmetic advantage (hidden scared surgery). For nipple areolar complex preserving mastectomy, small incision is only enough to circumareolar and 3 cm sized curved axillary incision. Long term follow up loco-regional recurrence data after endoscopy-assisted surgery about breast cancer little reported, so that we report our hospital's experience.
Methods: Between January 2006 and December 2009, total 90 case as breast cancer was treated by surgery Kwandong University Myongji hospital. Of the total 90 cases, 46 cases of treated by endoscopy assisted surgery were included in this study. The cases was followed up by June 2012 and their clinical characteristics and imaging study and pathologic data collected and reviewed retrospectively.
Results: Endoscopy-assisted breast conserving surgery (BCS) performed in the 32 patients and nipple areolar complex preserving mastectomy (NAC) performed in 14 patients. The median age of patients at the time of diagnosis was 48.4 year (range 34–65). The median follow up period is 45.5 months (range 30–71). Sentinel node biopsy using gamma-probe performed in 43 cases, further axilla lymph node dissection doned in 5 cases. Initial standard axillary lymph node dissection in the 3 cases. According to AJCC TNM staging, Stage 0 was 3, stage I was 24, Stage IIA was 12, stage IIB was 4, Stage IIIA was 2, Stage IIIB 3b 1. During above follow up period, the breast cancer related mortality was absent (0%), but one patient died because ovarain cancer metastasis (no related hormanal therpay). Locoregional recurrence in two cases (4.3%). Local recurrence developed in one case who took endoscopy-assisted BCS and radiotherapy after 24 months, modified radical mastectomy done. In one another case, ipsilateral axillary and inflaclavicular lymph node metastasis developed after 13 moths following taken NAC preserving mastectomy and sentinel node biopsy, axilla lymph node dissection doned.
Conclusion: Endoscopy-assisted surgery is available in not only the early but also locally advanced breast cancer, especially have a satisfactory result in cosmetic respects. Also Our Loco-regional Recurrence rate is lower than recurrence rate of other previous reports after BCS and NAC preserving mastectomy.
Disclosure of Interest: No significant relationships.

P193
COMPARATIVE STUDY OF LIPOMODELLING IN IMMEDIATE AND DELAYED BREAST RECONSTRUCTION
Y.S. Ahmed*. *Surgical Department, Medical Research Institute, Alexandria, Egypt*

Goals: Breast cancer treatment is now currently evaluated on cure-rate figures and quality of life. Reconstructive surgery in breast cancer patient aiming at decreasing the disabling effects of the ablative surgery. Oncoplastic techniques, autologous flaps and implants are commonly used in plastic surgery techniques in patients undergoing breast reconstruction. Lipomodelling is the process of relocating autologous fat to change the shape, volume, consistency and profile of tissues, with the aim of reconstructing, rejuvenating and regenerating body features Restoring an acceptable appearance after breast cancer surgery has become an integral part of the treatment process Even though advances in autologous and implant-based surgical techniques have greatly improved breast reconstructions over the past decennia, lipofilling, is already a practical application in reconstructive surgery of the breast that fulfills an ever-growing clinical demand. Aims of the study:
- Evaluate the feasibility of lipomodelling in immediate and delayed breast reconstruction following mastectomy and breast conservative surgery.
- Determine the esthetic and psychological outcome following lipomodelling.

Methods: This study was carried out on 40 patients with operable breast cancer admitted to the surgical department of Medical Research Institute Hospital, Alexandria University, Egypt. All patients will undergo either modified radical mastectomy (MRM) or breast conserving surgery (BCS) and will be subdivided into 2 groups: Group A: 20 patients will undergo immediate lipomodelling. Group B: 20 patients will undergo delayed lipomodelling. Both groups will undergo iterative (staged) lipomodelling (about 3 sessions) using collman technique. All patients will have to sign an informed consent that presented potential complications of infiltrating fat into the breast and also agree to undergo routine postoperative mammography and ultrasonography.
Results: Mean fat tissue injected after BCS (immediate and delayed) was 121 cc and in MRM (immediate and delayed) was 263.3 cc. Mean patients' satisfaction grade was 8.4/10 after BCS and 6.7/10 at MRM. Immediate complications included liponecrosis and infection in seven cases (17%) that required only dressings and oral antibiotics administration.
In cases of fat grafting after CBS, only four patients (10%) showed minor changes in the postoperative mammograms, consisting of the appearance of benign macrocalification and oil cyst.
Conclusion: Lipofilling technique is reliable method for restoration the shape and softness of the breast without surgical implant or flap reconstruction and with few side effect in the form of liponecrosis and infection. It easy method not need long training, cheap method without donor site complications and widely accepted by the patients.
Disclosure of Interest: No significant relationships.

Adjuvant systemic therapy

P195
EFFECTIVENESS OF ADJUVANT CHEMO/HORMONOTHERAPY IN INVASIVE LOBULAR CARCINOMA OF THE BREAST
O. Abdelrhman*, R. Abdelmalek, N. Kamal, H. Azim. *Oncology, Cairo Oncology Centre, Cairo, Egypt*

Goals: Most breast cancer research conclusions are driven by the outcome of patients with IDC. So, we have carried out a study of the features of Invasive Lobular Carcinoma (ILC) patients treated at our centre.
Methods: BC patients treated at Cairo Oncology Centre (Cairo, Egypt) in the period between2000–2008 were reviewed. Eligible patients were those who had no evidence of metastasis at diagnosis, and complete information on date of diagnosis, treatment, estrogen receptor (ER), progesterone receptor (PR) and HER2 status.

We compared the difference in systemic adjuvant therapy and pathological parameters between cases of invasive lobular carcinoma (ILC) and cases of invasive ductal carcinoma (IDC). We investigated the impact of HISTOLOGICAL SUBTYPE on disEASE free survival (DFS) in a Cox regression model adjusted for tumor size (pT), nodal status (pN), grade, ER, PR, HER2 and treatment. Finally, we evaluated the differences in the response to chemotherapy and hormonotherapy among both treatment groups.

Results: This analysis suggests that ILC patients are more likely to be older than 35 years, have ER +ve/PR +ve/Her2neu-ve phenotype suggesting luminal A/B subtype of breast cancer, present with advanced T (T3,4) stage, and develop lung metastases.

Based on multivariate analysis, the following variables were associated with shorter Disease Free Survival (DFS) in the population with ILC; Advanced T stage (HR = 2.23, p = 0.0001) nodal involvement, (HR = 1.87, p = 0.001). ER negativity (HR = 1.75, p = 0.0001) and not receiving chemotherapy (HR = 2.65, p = 0.001).

When the analysis was restricted to ER positive group, the following factors were significant in multivariate analysis for shorter DFS: Not receiving hormonal treatment (HR = 3.942, p = 0.0001), not receiving chemotherapy (HR = 2.82, p = 0.0001), nodal involvement (HR = 1.37, p = 0.003) and advanced T stage (HR = 1.75, p = 0.0001).

Conclusion: According to our data, adjuvant chemotherapy is effective in both ER positive and negative ILC, and cases of ILC should follow the same principles of adjuvant chemotherapy applicable to other subtypes of breast cancer.

Disclosure of Interest: No significant relationships.

P196

PREVENTION OF TAMOXIFEN-RELATED ENDOMETRIAL PATHOLOGY WITH LEVONORGESTREL INTRAUTERINE SYSTEM

W. Yeo[1]*, A. Wong[2], S. Chan[2], M. Yu[3], J. Suen[1], W.H. Tam[2].
[1]*Clinical Oncology, Chinese University of Hong Kong, Hong Kong, China,* [2]*Obstetrics and Gynaecology, The Chinese University of Hong Kong, Hong Kong, China,* [3]*Anatomical and Cellular Pathology, Chinese University of Hong Kong, Hong Kong, China*

Background and Objectives: The incidences of endometrial polyps and hyperplasia had been reported to be 5–35% and 4.7–16% respectively amongst tamoxifen users. Tamoxifen also increases the risk of endometrial cancer by 2-fold. A recent systematic review suggested that Levonorgestrel intrauterine system (LNG-IUS) is effective in inducing regression of endometrial hyperplasia. The objective of this study is to assess the role of prophylactic use of LNG-IUS in preventing endometrial pathology in breast cancer patients treated with tamoxifen.

Methods: This is a prospective randomized controlled trial. Main eligibility criteria were female breast cancer patients who required adjuvant tamoxifen. Prior to commencement of tamoxifen, patients were randomized to treatment (prophylactic LNG-IUS insertion) or control arm. Uterine cavity was examined by transvaginal ultrasound, hysteroscopy and endometrial sampling before, and at 12, 24, 45 and 60 months after commencement of tamoxifen. Any endometrial polyps or submucosal fibroids were resected through hysteroscopy; specimens were sent for histological confirmation by a histopathologist blinded to the randomization. This trial was registered under a Partner Registry of WHO International Clinical Trials Registry Platform.

Sample size calculation and statistical analysis: Assuming a dropout rate of 20%, 63 women were required in each arm to detect a 20% reduction in endometrial pathology with LNG-IUS at 5 years after the tamoxifen treatment with a power of 80% and type I error of 5%. Main outcome measures were de novo endometrial pathology during the 5 years of tamoxifen treatment.

Results: 129 patients were randomized; 64 in LNG-IUS arm and 65 in control arm. 80% completed 5-year follow-up. LNG-IUS was removed in 5 subjects due to intolerability. LNG-IUS significantly reduced de novo endometrial polyps (4.3% vs. 32.7%, p < 0.001; HR 0.19, 95% CI 0.07–0.48). There was no significant difference in the occurrence of endometrial thickness, submucosal fibroids, endometrial hyperplasia and endometrial cancer between the two groups. Based on intention-to-treat analysis, there was no difference in 5-year breast cancer recurrence (17.2% vs. 10.0%, p = 0.25) and mortality (10.3% vs. 8.3%, p = 0.71).

Conclusion: Prophylactic LNG-IUS prevents de novo endometrial polyps in women on tamoxifen.

Disclosure of Interest: No significant relationships.

P197

PERSISTENCE AND DISCONTINUATION OF ADJUVANT ENDOCRINE THERAPY IN JAPANESE WOMEN WITH BREAST CANCER

S. Kuba[1]*, M. Ishida[1], T. Shigechi[1], A. Igawa[1], A. Saruwatari[1], S. Nishimura[1], Y. Nakamura[1], K. Nishiyama[2], K. Taguchi[2], S. Ohno[1].
[1]*Breast Oncology, National Kyushu Cancer center, Fukuoka, Japan,* [2]*Pathology, National Kyushu Cancer Center, Fukuoka, Japan*

Goals: While adjuvant endocrine therapy improves the prognosis for women with hormone receptor-positive breast cancer, a certain number of them can't continue to receive the therapy for 5-year. Currently, little is known about persistence and discontinuation of adjuvant endocrine therapy in Asia. Thus, we sought to determine the frequency and reasons of discontinuation of endocrine therapy at a single institution in Japan.

Methods: We reviewed the medical records of 688 patients with hormone receptor-positive breast cancer who were treated with adjuvant endocrine therapy at the National Kyushu Cancer Center between 2001 and 2006. We defined "persistence" as the continuation of therapy, even when the physician ceased treatment because of recurrent disease or severe adverse effects. "Discontinuation" was defined as discontinuing therapy because of the patient's wishes.

Results: Among 688 patients who began to receive adjuvant endocrine therapy, 610 patients (89%) were classified as persistence with 517 (85%) fully completing the endocrine therapy course. Seventy-eight patients (11%) discontinued treatment. Reasons for discontinuation included side effects (46%), stopping visiting (33%), stopping taking medicine without any particular reason given to the physicians (14%), desire to get pregnant (5%) and financial reasons (1%). Seventy-eight percent of patients who discontinued therapy did not begin alternate treatment. Persistence was not correlated with age, menopausal status, tumor size, histological grade or adjuvant chemotherapy. Significant differences in clinico-pathological characteristics between patients who continued or discontinued treatment were lymph node metastases [35% and 24%, respectively (p = 0.002)], the rate of radiotherapy following lumpectomy [81% and 65%, respectively (p = 0.003)]. There was no difference, however, in five-year distant relapse-free survival between the persistence and discontinuation groups (90% and 93%, respectively), which might be related to the difference in lymph node metastasis rates.

Conclusion: Although the persistence rate of adjuvant endocrine therapy was high, approximately ten percent of the patients decided to discontinue treatment because of side effects, stopping visitation or without any particular reason. Therefore, important factors to decrease discontinuation of the therapy must be optimal information given to the patients about risk and benefit of the therapy and careful follow-up during the outpatient clinic.

Disclosure of Interest: No significant relationships.

P198
ADJUVANT HORMONAL THERAPY IN PREMENOPAUSAL BREAST CANCER: RESULTS FROM AN ITALIAN SURVEY

S. Barni[1]*, D. Amoroso[2], E. Collovà[3], K. Borgonovo[1], A. Frassoldati[4]. [1]*Medical Oncology, A.O. Treviglio-Caravaggio, Treviglio, Italy,* [2]*Medical Oncology, AUSL 12 Viareggio, Lido di Camaiore, Italy,* [3]*Oncology, A.O. Ospedali Civili di Legnano, Legnano, Italy,* [4]*Oncology, Clinica A.O. Universitaria di Ferrara, Ferrara, Italy*

Goals: The increasing age of first pregnancy among Italian women and the number of available therapy in premenopausal patients make adjuvant hormonal therapy an hot topic justifying a survey on the therapeutical approach of Italian oncologists to breast cancer.
Methods: From April to July 2012 a 11 items electronic questionnaire was submitted to italian oncologists and 611 filled questionnaires were collected, 294 M and 317 F, age range 25–65, 211 from north Italy, 173 from centre and 227 from south; 495 from general hospitals, 116 from research institutes. The results were examined globally and according to sex, age, working institution and geographical origin of the oncologists.
Results: 97.7% of patients aged less than 40 years needing only hormonal therapy would receive both tamoxifen (TAM) and LHRH analogue (LHRHa); 2.3% TAM or LHRHa alone. 93.6% of patients aged over 40 years would receive the combination with TAM or LHRHa offered to a greater number of women (6.4%). When LHRHa would be added to TAM the treatment length would be: 5 years in 60% and 44%, 3 years in 20.8% and 26.4%, 2 years in 19.2% and 29.6%, in patients aged under and over 40 respectively. The presence of at least one risk factors like positive nodes, high ki-67, G3, vascular invasion, HER2 3+, influence neither the therapeutic options nor the length of LHRHa use. In patients aged under 40 with chemotherapy induced amenorrhea, the oncologists would prescribe: TAM in 22.4%, TAM and LHRHa in 68.1% (LHRHa for 5 years in 55.3%, for 3 years in 22.1%, for 2 years in 22.6%), aromatase inhibitor (AI) +/− LHRHa in 6.6%, LHRHa alone in 2.9%. A greater number of patients would be treated with AI among women aged over 40 (11%). The reasons to add LHRHa toTAM and the length of treatment would be: higher efficacy of the combination: 45.5%; patient's age: 30.1%; risk of recurrence: 20.8%; and side effects: 3.6%. No difference was noted in questionnaire responses as regards sex, age, geographical origin and working institutes of the oncologists.
Conclusion: A high concordance between the Italian Oncologist attitude and the 2011 St. Gallen Guidelines is confirmed by this large survey. However, a wide preference for a TAM/LHRHa combination is reported, as well as a significant preference for LHRHa and AI combination in women below 40 years with chemotherapy induced amenorrhoea.
Disclosure of Interest: The survey was supported with unrestricted grant by Ipsen Italia.

P199
BONE TURNOVER IN GOSERELIN AND TAMOXIFEN TREATED PREMENOPAUSAL PATIENTS IN AN ADJUVANT TRIAL

A. Sverrisdottir[1]*, J. Gross[2], H. Johansson[1], H. Jacobsson[3], T. Gustafsson[4], S. Rotstein[1], T. Fornander[1]. [1]*Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden,* [2]*Department of Endocrinology, Sodersjukhuset, Stockholm, Sweden,* [3]*Radiology, Karolinska Institutet, Stockholm, Sweden,* [4]*Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden*

Goals: To examine if changes in bone turnover markers (BTM) in premenopausal breast cancer patients receiving adjuvant endocrine treatment, may be useful for early detection of risk for accelerated bone loss, in order to monitor bone health and prevent osteoporotic fractures.
Methods: Patients from two centres in the Stockholm cohort of the Zoladex in Premenopausal Patients (ZIPP) trial, were recruited to a study of bone markers. Patients were randomly allocated to goserelin, goserelin in combination with tamoxifen, tamoxifen alone or no endocrine treatment. The bone markers osteocalcin (OC), pyridinoline cross-linked amino terminal telopeptide of type I collagen (PINP) and C-terminal telopeptide (CTX) were examined.
Results: Bone marker analyses from a total of 50 women were available at baseline and after 6 months of treatment. Among women treated with goserelin, there was a significant rise in OC (RR: 1.57, $p < 0.001$), PINP (RR 1.65, $p = 0.001$) and CTX (RR 1.98, $p < 0.001$). There were no significant changes in BTM among those treated with either goserelin and tamoxifen or tamoxifen alone. Among patients where bone mineral density measurements were available, Spearman correlation analysis showed that change in BMD was associated with change in in all bone markers ($r = -0.40$ to -0.51).
Conclusion: The LHRH agonist goserelin significantly increases BTM in premenopausal breast cancer patients. Tamoxifen seems to neutralize the effect of goserelin in regard to BTM. There is a significant inverse correlation between change in BMD and BTM among endocrine treated patients. Bone markers in addition to BMD may be useful in identifying women at risk for bone loss, monitoring bone health and make early interventions possible.
Disclosure of Interest: The author received a grant from Astra-Zeneca for bone markers assays. The author receives travel support from Novartis to the present meeting.

P200
RETROSPECTIVE ANALYSIS OF TREATMENT DECISIONS IN PATIENTS WITH INTERMEDIATE RECURRENCE SCORE RESULTS

G. Fried*, M. Moskovitz. *Oncology, Rambam Health Care Campus, Haifa, Israel*

Goals: The Oncotype DX® assay is validated as a prognosticator and a predictor of likelihood of chemotherapy benefit in ER positive early breast cancer (ERBC). Patients (pts) with high Recurrence Score results have significant benefit from chemotherapy and pts with low Recurrence Score results have minimal, if any benefit. Some pts with intermediate Recurrence Score results may have a moderate benefit from chemotherapy, increasing the importance of considering other clinical and pathological parameters associated with risk of recurrence in order to optimize treatment decisions. The aim of this study was to assess the impact of intermediate Recurrence Score results and other factors on treatment decisions.
Methods: A retrospective study of ERBC with intermediate Recurrence Score results treated between 2005 and 2010 in a single institution was performed and identified 116 pts. The physician's recommendations prior to knowing the Recurrence Score results were consistently recorded and clinicopathological features and treatment decisions were obtained from pts' records. Five patients had missing data and were excluded.
Results: Before receiving the Recurrence Score result, 33 pts (29.7%) were recommended chemo-hormonal therapy (CHT) and 78 pts (70.3%) were recommended hormonal therapy (HT) alone. After receiving the Recurrence Score result, 13/33 (39%) pts originally recommended CHT received HT and 11/78 (14%) of pts originally recommended HT received CHT. Overall, 24/111 (22%) pts received different treatment than that recommended prior to knowing the Recurrence Score result. Pts who received CHT ($n = 30$) had higher Recurrence Score results and younger mean age than those who received HT ($n = 81$). The change rate was similar in grade 2 (24.1%) and grade 3 (27.3%), but lower in grade 1 tumors (6.6%) ($p = 0.27$). There was a trend ($p = 0.06$) towards larger tumor size in CHT-recommended pts compared to HT-recommended pts.
Conclusion: A clinically relevant proportion of pts with intermediate Recurrence Score results had a change in treatment decisions

demonstrating that clinicians considered intermediate Recurrence Score results to be informative. Younger pts and pts with higher intermediate scores tended to be recommended CHT and pts with lower intermediate scores tended to be recommended HT alone. Changes occurred in all grades but were more likely in grade 2 and 3 tumors.

Disclosure of Interest: No significant relationships.

P201

FORMATION OF MULTICELLULAR TUMOR SPHEROIDS BY MCF-7 AND SENSITIVITY TO ANTICANCER THERAPY

D. Demianenko*, O. Perepelytsina, T. Gergeliuk, M. Sydorenko. *Department for Biotechnical Problems of Diagnostic, Institute for problems of cryobiology and cryomedicine NAS Ukraine, Kiev, Ukraine*

Goals: One of the factors that hinder early diagnosis and treatment of breast cancer is metastasizing. Another one is changing in expression of hormone-dependent receptors, which is accompanied by the loss of sensitivity to anti-hormonal anticancer therapy. Therefore the aim of study was to investigate the influence of estradiol, progesterone, interferon alpha and gamma on the formation of tumor microaggregates (MTS), Estrogen receptor profile of tumor cells and the sensitivity to anticancer therapy (tamoxifen – TAM).

Methods: As an experimental model system were used breast adenocarcinoma cells, MCF-7. 3D culture of multicellular tumor spheroids were obtained using the modified by authors method of Jens M. Kelm. Recombinant IFN-γ was added in concentration of 103 U/ml, IFN-α – 10 U4/ml, TAM – 100 nM, estradiol (E2) – 10 nM, Pr – 10 nM. Cell survival was determined by MTT test [Mosmann T., 1983]. Expression of ER was visualised by immunocytochemistry (DAKO, USA). The size of multicellular spheroids was assessed by photographing and measurement by image processing program (Stemi2000, Zeiss) with conversion formula of R. Bjerkvig.

Results: Our results indicated that E2 and IFN-γ are the agents that stimulate cell proliferation, survival and formation of MTS. At the same time level of ER expression increased and sensitive cell to TAM was decreased. In suspension fraction cell number increased with E2, IFN-γ + E2, TAM + E2 and IFN-γ + TAM. Decreasing the cell number in suspension fraction was demonstrated for samples with Pr, IFN-γ and TAM. While in adhesion fraction with TAM, TAM + E2 decreased the number of alive cells. The largest size and the number of MTSs were observed in culture with E2 and IFN-γ. IFN-α and Pr demonstrated cytostatic properties and capacity to reduce MTS formation. IFN-γ and Pr reduced the survival of tumor cells in the spheroids. The number of MTS after incubation with Pr and IFN-α was in 25 and 3 times less than in control.

Conclusion: Thus, our data demonstrated that cell microenvironmental conditions (hormonal and humoral) have a strong influence on ER expression in breast cancer cell and as a result can modulate sensitiveness to antiestrogen therapy. Combination of antiestrogen therapy with balanced approach of IFN-α, IFN-γ and level of E2/Pr may have cumulative effect in antitumor treatment.

Disclosure of Interest: No significant relationships.

P202

SAFETY OF METRONOMIC CAPECITABINE THERAPY FOR EARLY TRIPLE NEGATIVE BREAST CANCER (SYSUCC-001 TRIAL)

X. Wang[1]*, Z. Yuan[2], D. Liu[2], S. Wang[3], L. Zhao[4], C. Zhang[5], Q. Chen[6], X.-M. Wang[7], H. Huang[8], J. Zeng[9]. *[1]Departments of Breast Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China, [2]Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China, [3]Sun Yat-sen University Cancer Center, Guangzhou, China, [4]The First People's Hospital of Guangzhou, Guangzhou, China, [5]General Hospital of PLA Guangzhou Military Area, Guangzhou, China, [6]Traditional Chinese Medicine Hospital of Guangdong Province, Guangzhou, China, [7]Shenzhen Second People's Hospital, Shenzhen, China, [8]Lianjiang City Pepole's Hospital, Lianjiang, China, [9]The First Affiliated Hospital of Guangxi Medical University, Guangxi, China*

Goals: To compare disease-free survival (DFS) of TNBC patients who were randomized to treatment with either standard adjuvant chemotherapy alone or standard adjuvant chemotherapy followed by 1 year of metronomic capecitabine therapy.

Methods: After standard adjuvant chemotherapy, TNBC patients were randomized to receive continuous lower dose capecitabine for one year, or observation only. Study primary endpoint is 3-year disease-free survival (DFS).

Results: As of November 2012, 186 patients from seven centers in China have been randomized (94 in capecitabine group, 92 in observation group); here we report safety data for these 186 patients. Recruitment to the study is currently ongoing with accrual of 424 patients planned. Patient baseline demographics and disease characteristics are well balanced between two groups. Median age is 45 years (range 26–65). More than seventy percent of patients were premenopausal. More than half of the patients were at stage I/II. The majority of patients had received previous adjuvant treatment with anthracycline and taxane. The planned dose of metronomic capecitabine was 650mg/m2 twice daily for continuous for one year. In capecitabine arm, 39 patients complete done-year treatment. Of 94 patients, only 3 patients (3.2%) had a dose modification, 2 patients had a reducing dose due to hand-foot syndrome or delays, one patient had a delaying dose due to gastrointestinal pain. The majority of adverse events were grade 1/2. No grade 3/4 capecitabine-related clinical adverse events were observed in all treated patients. The most common capecitabine-related clinical adverse events were hand-foot syndrome (8.5%) and gastrointestinal pain (6.4%). There were more disease relapse in observation group (n = 7) than in capecitabline group (n = 3).

Conclusion: The rationale for evaluating metronomic capecitabine in TNBC is supported by experimental and clinical data. Most common adverse events are hand-foot syndrome and gastrointestinal pain. The safety profile of metronomic capecitabine as adjuvant therapy is lower, manageable and consistent with its known toxicity profile.

Disclosure of Interest: No significant relationships.

P203

THERAPEUTIC DRUG MONITORING OF DOCETAXEL FOR A LIVING DONOR LIVER TRANSPLANTATION RECIPIENT

K. Kawaguchi[1]*, H. Ishiguro[2], I. Yano[3], H. Yamashiro[4], M. Toi[1]. *[1]Department of Breast Surgery, Kyoto University Hospital, Kyoto, Japan, [2]Outpatient Oncology Unit, Kyoto University Hospital, Kyoto, Japan, [3]Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan, [4]Department of Breast Surgery, National Hospital Organization Kure Medical Center, Hiroshima, Japan*

Goals: Therapeutic drug monitoring (TDM) provides valuable guidance for the dose adjustment of several classes of drugs especially when the pharmacokinetics and pharmacodynamics are not predictable. Recently, we have had an opportunity to administer a docetaxel for a breast cancer patient who is a living donor liver

transplantation (LDLT) recipient with severe renal dysfunction using TDM strategy.

Methods: Blood samples were obtained prior to docetaxel infusion, immediately before the end of infusion and 10, 30, 60, 120 and 180 min after the end of infusion. Pharmacokinetic parameters were calculated with the software WinNonlin using the two-compartment model. An informed consent was obtained for participation into the pharmacokinetics study of docetaxel, which was approved by the Ethics Committee of Kyoto University Graduate School of Medicine.

Results: The 63-year-old woman presented to us in September 2008 with cT2N1M0 invasive ductal carcinoma of the breast, triple negative phenotype. She received LDLT at age 58 due to hepatitis B. The donor was her husband. She has been taking tacrolimus, cilnidipine and lamivudine after transplantation. She suffered renal dysfunction (serum creatinine 2.0 mg/dl, creatinine clearance 30 mL/min) attributed to the tacrolimus and her recent serum liver enzymes were within upper normal limits. We have administered 40 mg/m^2 of docetaxel through the use of TDM. The area under the blood concentration-time curve (AUC) and clearance (CL) of docetaxel in the first cycle were 0.91 mg*h/L and 61.8 L/h, respectively. Compared to the pharmacokinetics data from our clinical trial reported recently, CL in the current patient was about 1.8 times higher, and with a target AUC of around 3 mg*h/L in accordance with a phase 3 study, dose escalation of docetaxel up to the maximum tolerated dose of 100 mg/m^2 seemed feasible through the use of TDM. We started the second cycle on day 15 of first cycle at an increased dose of 75 mg/m^2. Non-hematologic toxicity was not observed and the nadir neutrophil count on day 8 was 600 cells/mm^3. After increasing the third cycle dose to 100 mg/m^2, the nadir neutrophil count on day 8 of the third cycle was 300 cells/mm^3 and only grade 1 non-hematological toxicities were observed.

Nadir neutrophil count and non-hematological toxicity in each cycle

Docetaxel dose	Cycle	Nadir neutrophil count	Non-hematological toxicity
40 mg/m^2	1st	1900 cells/mm^3	Grade 0
75 mg/m^2	2nd	600 cells/mm^3	Grade 0
100 mg/m^2	3rd	300 cells/mm^3	Grade 1

Conclusion: Little is known about the pharmacokinetics of antineoplastics, including docetaxel, in LDLT recipients. Given our experience here, TDM for antineoplastics indeed provides valuable guidance for dose adjustment in such patients when the pharmacokinetics and pharmacodynamics are not predictable.

Disclosure of Interest: No significant relationships.

P204

OVERCOMING CYP2D6-MEDIATED TAMOXIFEN RESISTANCE: PHENOTYPE-SPECIFIC TAMOXIFEN–ENDOXIFEN COMBINATIONS

K. Dickschen[1] *, T. Eissing[2], T. Mürdter[3], M. Schwab[3], S. Willmann[2], G. Hempel[1]. [1]*Institute for Pharmaceutical and Medical Chemistry; Clinical Pharmacy, University of Münster, Münster, Germany,* [2]*Computational Systems Biology, Bayer Technology Services GmbH, Leverkusen, Germany,* [3]*Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology and University Tuebingen, Stuttgart, Germany*

Goals: Tamoxifen (TAM) is a mainstay of treating estrogen-receptor positive breast cancer. The secondary metabolite of TAM, endoxifen (END), is regarded as a major contributor to its anti-tumoral activity. Patients with an intermediate or poor metabolizer (IM, PM) phenotype of cytochrome P450 2D6 (CYP2D6), a major enzyme in END formation, show a decrease in END plasma levels. There is convincing evidence that these patients may not fully benefit from regular TAM therapy. Genotype-guided TAM dose escalation or END mono-therapy are currently investigated as new treatment strategies for IMs and PMs to achieve END levels similar to extensive metabolizers (EMs) under regular TAM therapy. The presented virtual clinical trial aims to establish a dose guideline that achieves the long proven and highly beneficial EM-specific TAM-metabolite pattern also in IMs and PMs.

Methods: A previously validated CYP2D6 phenotype-specific physiology-based pharmacokinetic (PBPK)-model describing TAM and its main metabolites was applied in the virtual clinical trial. In study group A, TAM standard dosing (20 mg/d) was simulated in EMs, IMs, and PMs. Results were compared to data from five clinical trials. In study group B, TAM dose escalation was simulated in IMs and PMs. Results were compared to the EM reference group of study group A and clinical data. In study group C, dose combinations of TAM (20 mg/d) and END (0.5–4.0 mg/d) were simulated in IMs and PMs. Results were compared to the EM reference group of study group A.

Results: The PBPK-model nicely reflects the plasma levels of TAM, N-desmethyltamoxifen (NDM), 4-hydroxytamoxifen (4OH), and END reported in the literature for the dosing scheme applied in study group A. Dose escalation of TAM in IMs results in END steady-state plasma levels comparable to the EM reference group in study group A and clinical data. TAM dose escalation in PMs does not achieve standard END EM levels up to doses of 60 mg/d. In both cases, TAM and NDM plasma levels are much higher compared to the EM reference group. IMs achieve steady-state plasma levels of TAM, NDM, 4OH, and END similar to the EM reference group when receiving a combination of 20 mg/d TAM and 1 mg/d END. The same applies for PMs receiving 20 mg/d TAM and 3 mg/d END.

Conclusion: Combined administration of TAM and END in patients with impaired CYP2D6 enzyme activity could be a promising new strategy for these patients.

Disclosure of Interest: The authors acknowledge financial support by the BMBF for the grant 0315747 (Virtual Liver) and the Robert Bosch Foundation, Stuttgart, Germany. KD and GH are funded by and TE and SW are employees of BTS, the company that owns the software used for the si

P205

HIGH-RISK LUMINAL BREAST CANCER PATIENTS TREATED WITH ENDOCRINE THERAPY ALONE

T. Seki[1] *, A. Matsumoto[1], T. Murata[1], A. Nagayama[1], M. Takahashi[1], T. Hayashida[1], H. Jinno[1], Y. Kitagawa[1], H. Shigemichi[2]. [1]*General Surgery, Keio University, Tokyo, Japan,* [2]*Pathology, Keio University School of Medicine, Tokyo, Japan*

Goals: Recent studies showed that luminal breast cancer exhibited lower sensitivity to chemotherapy than other subtypes. The aim of this study is to evaluate the characteristics of high-risk luminal breast cancer patients who can be treated with endocrine therapy alone.

Methods: Among 2070 breast cancer patients who had surgery and adjuvant treatment at Keio University hospital from January 2003 to October 2012, 1426 (69.0%) patients had estrogen receptor (ER)-positive and/or progesterone receptor (PgR)-positive/HER2-negative breast cancer. 251 (12.1%) out of 1426 patients with ER and/or PgR-positive/HER2-negative breast cancer had pathological positive axillary lymph nodes. Hormone receptor (HR) status was assessed by immunohistochemistry (IHC) and determined using the Allred score. HER2 status was assessed by IHC and fluorescence in situ hybridization (FISH) analysis.

Results: Out of 251 luminal patients, 47 patients were treated with endocrine therapy alone (group H) and 204 patients were treated with chemotherapy in addition to endocrine therapy (group HC). After a median-follow up of 61 months, we observed recurrence in 3 patients (6.4%) of group H and 39 patients (19.1%) of group HC (HR = 2.99, p = 0.051). Five-year recurrence rate was 0.96 for group H and 0.84 for group HC (p = 0.021). The median age was significantly higher in group H compared with group HC (65 years vs. 52 years, p < 0.001). The median clinical tumor size was significantly smaller in

group H compared with group HC (2.47 cm vs. 3.57 cm, $p < 0.001$). The mean pathological tumor size was 1.86 cm for group H and 1.92 cm for group HC ($p = 0.185$). The number of clinical N0 patients was also significantly higher in group H compared with group HC (74.5% vs. 64.3%, $p < 0.001$). The numbers of pathological positive axillary lymph nodes tended to be higher in group HC compared with group H (2.6 (range 1–6) vs. 3.6 (range 1–49), $p = 0.28$). There were no significant differences in nuclear grade (NG), and lymphovascular invasion. NG3 was found in 4 patients (8.5%) of group H and 16 patients (7.7%) of group HC. Intensely positive lymphatic invasion was found in 3 patients (6.4%) of group H and 29 patients (14.0%) of group HC. Positive vascular invasion was found in 2 patients (4.3%) of group H and 17 patients (8.2%) of group HC. The number of patients with high ER levels (Allred 7–8) was higher in group H than group HC (76.6% vs. 61.3%, $p = 0.34$).

Conclusion: These data suggested that high-risk luminal breast cancer patients might be treated with adjuvant endocrine therapy alone, when the patients are elderly and had a limited tumor burden.

Disclosure of Interest: No significant relationships.

P206

ADJUVANT TC (DOCETAXEL/CYCLOPHOSPHAMIDE)-HER (TRASTUZUMAB) (TC-HER) IN HER2 POSITIVE BREAST CANCER

F. Hara*, S. Kiyoto, M. Takahashi, D. Takabatake, S. Takashima, K. Aogi, S. Ohsumi. *Breast Oncology, Shikoku Cancer Center, Matsuyama Ehime, Japan*

Goals: Trastuzumab improves survival in the adjuvant treatment of HER-positive breast cancer, although the addition of trastuzumab to anthracycline-containing regimens is associated with increased cardiac toxicity. TC is an effective adjuvant chemotherapy regimen in early stage breast cancer regardless of intrinsic subtype. Therefore we sought to evaluate the efficacy and safety of TC-HER, non-anthracycline regimen with trastuzumab in low-risk HER2-positive breast cancer.

Methods: Patients with low-risk HER2-positive breast cancer at Shikoku Cancer Center received docetaxel (T) 75 mg/m^2 and cyclophosphamide (C) 600 mg/m^2, plus trastuzumab (HER) 8 mg/kg (loading dose) and 6 mg/kg thereafter for a total of 4 cycles every 3 weeks. After 4 cycles of TC-HER, trastuzumab was administered every 3 weeks to complete 12 months of therapy with trastuzumab.

Results: At a median follow-up was 32.9 months, of the 90 patients treated with TC-HER, 78 (86.7%) patients completed one year of HER. Median age was 55 years (range: 22–70) and all patients had ECOG PS 0. 16.6% of patients had subcentimeter tumor and 17.8% had lymph node involvement (up to one positive node). 64.4% were estrogen receptor positive, 42.2% were progesterone receptor positive. The most common grade 3/4 hematologic toxicities were leukopenia 57.8%/28.9%, neutropenia 25.6%/68.9%, and febrile neutropenia 37.8%. G-CSF was administered to 6.7% patients. Skin rash, liver enzyme elevation, arthralgia, fatigue and stomatitis were the most common non-hematological toxicities and almost of all were grade2 or less. No patients had declines of LVEF below 50% during treatment. At a median follow-up of 32.9 months, one patient had local recurrence and all patients are alive.

Conclusion: Four cycles of the nonanthracycline TC regimen combined with 1 year trastuzumab is very effective and tolerable. The TC-HER regimen is one of the option for patients with in lower risk HER2 positive breast cancer as an adjuvant treatment.

Disclosure of Interest: No significant relationships.

P207

PATIENT PREFERENCE FOR SUBCUTANEOUS VERSUS INTRAVENOUS TRASTUZUMAB: RESULTS OF THE PREFHER STUDY

X. Pivot[1]*, J. Gligorov[2], V. Müller[3], S. Verma[4], A. Knoop[5], G. Curigliano[6], V. Jenkins[7], N. Scotto[8], S. Osborne[8], L. Fallowfield[7]. *[1]Chimiothérapie–Oncologie, CHU Jean Minjoz, Besançon, France, [2]APHP-Tenon IUC-UPMC, Paris, France, [3]University Medical Center, Hamburg, Germany, [4]Sunnybrook Odette Cancer Centre, Toronto, Canada, [5]Odense University Hospital, Odense, Denmark, [6]Division of Medical Oncology, European Institute of Oncology, Division of Medical Oncology, Milano, Italy, [7]Sussex Health Outcomes, Research & Education in Cancer (SHORE-C), Sussex, United Kingdom, [8]F. Hoffmann-La Roche Ltd, Basel, Switzerland*

Goals: To evaluate patient preference for subcutaneous (SC) versus intravenous (IV) trastuzumab administration in HER2-positive early breast cancer.

Methods: PrefHer is a randomised, multicentre, international clinical trial (NCT01401166). Primary endpoint: proportion of patients indicating an overall preference for SC versus IV trastuzumab (null hypothesis: 65% for SC against 2-sided alternative hypothesis). Secondary endpoints: healthcare professional (HCP) satisfaction, safety, event-free survival and immunogenicity. Exploratory endpoints included reasons for patient preference. After completing (neo)adjuvant chemotherapy, patients were randomised to receive 4 cycles of trastuzumab SC (fixed dose of 600 mg via single-use injection device [SID]) followed by four cycles of trastuzumab IV (8 mg/kg → 6 mg/kg) or the reverse sequence as part of their adjuvant trastuzumab therapy. Two study-specific patient interviews (PINTs) were developed using standard methods. Questions investigated factors potentially influencing preferences such as experiences during administration. Patients' final preferences, reasons for these and strength of preference were elicited. Experienced interviewers conducted telephone PINTs before and after the crossover period. Interviews were quality-controlled to ensure impartial questioning. Adverse events (AEs) were assessed by NCI-CTCAE V4; serious AEs (SAEs) by ICH E2A.

Results: Two hundred and forty-eight patients were randomised; 236 received trastuzumab SC and IV and completed both PINTs. The safety population ($n = 244$) received ≥1 dose of study drug. Baseline demographics/tumour characteristics/treatment history will be presented. Trastuzumab SC was preferred by 92% of patients (95% CI 87–95%; $p < 0.0001$), 7% preferred IV (95% CI 4–11%) and 2% had no preference (95% CI 1–4%). Of the patients who preferred SC, overall preferences were 'very strong' in 74%, 'fairly strong' in 21% and 'not very strong' in 6%. Primary reasons for SC preference were time saving and less pain/discomfort. AEs were reported in 69% of patients (63% grade 1, 34% grade 2, 6% grade 3, no grade 4/5, 3% SAEs) with no new safety signals.

Conclusion: Patients overwhelmingly (92%) preferred SC over IV trastuzumab. No safety differences were reported compared to the known profile of the IV formulation.

Disclosure of Interest: Relationships with Roche: XP: consultant. JG/AK: consultant/advisor, travel. VM: speaker honoraria, research funding. SV: consultant/advisor*; research funding. GC/VJ: None. NS: employee, shares. SO: employee. LF: advisor, research funding. *Also GSK

P208

BUDGET IMPACT ANALYSIS OF THE ONCOTYPE DX® BREAST CANCER TEST IN FRANCE

R. Rouzier[1]*, E. Laas[2], E. Chéreau[3], J. Gligorov[2]. *[1]Unité de Chirurgie Gynécologique et Sénologique, Institut Curie, Paris, France, [2]Hopital Tenon, Paris, France, [3]Institut Paoli-Calmettes, Marseille, France*

Goals: The Oncotype DX® assay is a diagnostic test that quantifies the likelihood of disease recurrence and likely benefit from adjuvant

chemotherapy in women with ER+, HER2−, pN0 early stage invasive breast cancer. The cost-effectiveness of this test is well established in multiple countries (Pronzato et al., 2011) including France (Vataire et al., 2012) but its budget impact is not as widely documented. However, budget impact analyses are extremely useful for healthcare payers to inform funding of healthcare technologies. This study objective was to estimate the likely budget impact associated with the introduction of the assay in French clinical practice.

Methods: An excel model was built to estimate the impact on the social security budget if the Oncotype DX® test was to be reimbursed in the eligible patient population (early stage ER+, HER2−, pN0 breast cancer patients) in the first year. Epidemiological data were collected from French national statistics. Assumption on the real-life use of the assay was adapted from a study of clinical patterns in the US (Hassett et al., 2012). Data describing the impact of using the Oncotype DX® test on chemotherapy decisions were collected from the French decision impact study (Gligorov et al., 2012). Chemotherapy cost data were collected from a French cost study (Laas et al., 2012). The list price of the Oncotype DX® test was used for the calculation. One-way sensitivity analyses were conducted on all parameters.

Results: In 2011, 53,000 new patients were diagnosed with breast cancer in France. It is estimated that without the Oncotype DX® test, 52% of those patients would be likely to receive chemotherapy leading to a total cost over €143 million. If the Oncotype DX® were to be reimbursed in France, 10,128 patients would be likely to benefit from it in clinical practice. The model estimates that over €37 Million could be saved by avoiding un-necessary chemotherapy. When taking into account the cost of the test, it is estimated that the social security could save over €5 million (€496 per patient tested) with the Oncotype DX® test. Sensitivity analyses showed that the budget impact results were most sensitive to the proportion of women receiving chemotherapy before and after the Oncotype DX® test and to the cost of chemotherapy.

Conclusion: If the Oncotype DX® test was to be reimbursed in France, it is estimated that a significant chemotherapy budget could be saved by the social security.

Disclosure of Interest: No significant relationships.

P209

TIME SAVINGS WITH TRASTUZUMAB SUBCUTANEOUS VS INTRAVENOUS ADMINISTRATION: A TIME AND MOTION STUDY

E. De Cock[1] *, Vladimir Semiglazov[2], G. López Vivanco[3], S. Verma[4], X. Pivot[5], J. Gligorov[6], N. Hauser[7], A. Urspruch[8], P. Kritikou[9], A. Knoop[10]. *[1]Peri- and Post-approval Services, United BioSource Corporation, Barcelona, Spain, [2]N.N. Petrov Research Institute of Oncology, St Petersburg, Russian Federation, [3]Hospital Universitario Cruces, Barakaldo, Spain, [4]Sunnybrook Odette Cancer Centre, Toronto, Canada, [5]Service Oncologie Médicale, CHU Jean Minjoz, Besançon, Besançon, France, [6]APHP-Tenon IUC-UPMC, Paris, France, [7]Kantonsspital Baden (AG), Baden, Switzerland, [8]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [9]UBC, London, United Kingdom, [10]Odense University Hospital, Odense, Denmark*

Goals: To quantify healthcare professional (HCP) time and cost for tasks related to trastuzumab (TRA) subcutaneous single-use injection device (SC SID) application vs. TRA intravenous (IV) infusion for the treatment of patients with HER2+ early breast cancer; to estimate potential time savings with a conversion from IV to SC SID; secondly to compare patient chair time (i.e. time between chair entry and exit).

Methods: A multi-centre (6 countries/17 centres), prospective, observational time and motion (T&M) study was run alongside the PrefHer trial (ClinicalTrials.gov id: NCT01401166). Generic case report forms for IV, SC SID, and pharmacy management were tailored to reflect local site practices. Trained observers recorded the duration that HCPs were actively completing pre-specified tasks, and separately patient chair time. Number of TRA patient sessions observed by country ranged from 11 to 95 and 13 to 94 for SC SID and IV, respectively. IV vs. SC SID process time per patient was calculated as the sum of the mean task times, and corresponding 95% confidence intervals (CIs) were based on the sum of the variances from each task. CIs were estimated assuming Gamma or Weibull distributions (selected based on goodness of fit). At study end, perceived impact on centre management due to a change in administration route was explored via a qualitative questionnaire (ongoing).

Results: Difference in mean HCP time for IV vs. SC SID processes ranged from 6.6 min (−28%) in Denmark (IV: 23.1 [95% CI: 15.8–30.4] vs. SC 16.5 [95% CI: 12.2–20.9]) to 15.5 min (−47%) in Russia (IV: 32.9 [95% CI: 27.6–38.2] vs. SC 17.4 [95% CI: 13.2–21.5]). Per treatment course (18 sessions), estimated time reduction ranged from 114 min in Denmark (414 vs. 300) to 250 min in Russia (592 vs. 312). Total HCP time savings were mainly attributable to reductions in nurse time in Spain, France and Russia (76%, 54%, and 50% of total reduction, respectively) and pharmacy technician time in Denmark (100%) and Switzerland (76%). Difference in mean chair time for IV vs. SC ranged from 58 min (−68%) in France (IV: 85 min vs. SC 27 min) to 81 min (−80%) in Spain (IV: 101 min vs. SC: 20 min).

Conclusion: Conversion from IV to SC SID TRA leads to a substantial reduction in administration chair time as well as in HCP time. Consequently, staff-efficiency can be increased as well as centre's capacity to treat more patients.

Disclosure of Interest: EC/PK: research commissioned by Roche. VS/GLV/NH: None. SV: Roche/GSK consultant/advisory role; Roche research funding. XP: Roche consultant. JG/AK: Roche consultant/advisory roles, travel. AU: Roche employee.

P210

JOINT SYMPTOMS IN CONTINUATION AND STOP GROUPS AFTER 5 YEARS OF ANASTROZOLE: NSAS-BC 05

K. Higaki[1] *, H. Ohtsu[2], H. Yagata[3], K. Shimozuma[4], Y. Komoike[5], S. Saji[6], H. Takei[7], T. Nakamura[8], Y. Ohhashi[2], T. Iwase[9]. *[1]Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan, [2]University of Tokyo, Tokyo, Japan, [3]St. Luke's International Hospital, Tokyo, Japan, [4]Ritsumeikan University, Kyoto, Japan, [5]Kinki University Hospital, Osaka, Japan, [6]Kyoto University Graduate School of Medicine, Kyoto, Japan, [7]Saitama Cancer Center, Saitama, Japan, [8]University of Occupational and Environmental Health School of Medicine, Fukuoka, Japan, [9]Cancer Institute Hospital, Tokyo, Japan*

Goals: To compare joint symptoms (pain and stiffness) at baseline (BL) and after 1 year (1Y) when the use of anastrozole is extended for 5 years after the completion of 5-year postoperative endocrine therapy in patients with postmenopausal breast cancer.

Methods: Patients registered in NSAS-BC 05 were asked to respond to validated health-related quality of life (HRQOL) instruments, which include joint symptoms (pain and stiffness), at BL and at 1Y. The subjects were 290 patients at 64 institutions from whom HRQOL surveys were collected at BL and at 1Y. There were 150 patients in the anastrozole continuation group (CNT group) and 140 patients in the stop group (STP group). The mean age was 64, and body mass index was below 25 in 75.5% of patients.

Results: Concerning joint pain, daily activities were affected due to severe pain in 3.1% at BL and 4.8% at 1Y in the CNT group, and in 3.1% at BL and 1.5% at 1Y in the STP group, showing no statistical difference. Assessment of the location of the joint pain showed an increased trend for elbow pain in both groups ($p = 0.0627$). Daily activities were affected due to stiffness in 0.6% at BL and 2.0% at 1Y in the CNT group, and in 1.9% at BL and 0% at 1Y in the STP group, showing no statistical difference. Assessment by location showed a statistically significant difference for the foot ($p = 0.0337$), thumb ($p = 0.0128$) and metacarpophalangeal joints (MCP) ($p = 0.0407$).

Conclusion: Only joint symptoms during the first year after the start of this study are examined here, but the anticipated worsening of

symptoms due to continuation of anastrozole and alleviation of symptoms due to stopping of anastrozole were not observed.
Disclosure of Interest: No significant relationships.

P211
TRIPLE NEGATIVE EARLY BREAST CANCER: SINGLE CENTRE EXPERIENCE IN ADJUVANT SETTING CHEMOTHERAPY

G.P. Giardina[1]*, B. Veronese[1], I. Marcon[1], I. Vallini[2], L. Bascialla[1], K. Milani[2], A. Ritorna[1], G. Pinotti[1]. *[1]Medical Oncology, Ospedale di Circolo e Fondazione Macchi, Varese, Italy, [2]Oncologia, Ospedale di Circolo, Varese, Italy*

Goals: Triple-negative breast cancer (TNBC) is an aggressive histological subtype with limited treatment options and very poor prognosis. Despite it shows a good response to chemotherapy but the optimal treatment is still in debate. The aim of the present study was to investigate retrospectively the role of anthracyclines in adjuvant setting. Distant and local TNBC recurrence was the main end point.
Methods: From our database we identified 129 patients (pts) with stage I-II TNBC diagnosed during 2000–2010 and treated with surgery +/− radiotherapy and Anthracyclines (100 pts – group A) or non Anthracyclines (29 pts – group B) based chemotherapy. 13 pts did not perform any chemotherapy treatment due to different co morbidity. TNBC is defined on surgical specimen as ICH ER−ve, PgR−ve and HER2−ve (FDA 0–1) or HER2 (FDA 2+)/FISH−ve.
Results: All 129 pts were ICH ER−ve, PgR−ve, 123 were HER2−ve (FDA 0–1) and 6 HER2 (FDA 2+)/FISH−ve. Median age of our pts was 53 yrs for group A and 59.5 yrs for group B. In group A there were 38 pts Stage I (38%) and 48 pts Stage II (48%) disease, while in group B Stage I were 8 pts (27.6%) and Stage II were 14 pts (48%). Median follow-up was 33.5 and 46.5 months respectively (range A [3–146]; range B [5–134]). In group A we have had 9 relapses (9 out of 100 pts; 9%) compared with 7 relapses in group B (7 out of 29 pts; 24%). The majority of relapsed pts (13/19; 68%) had lymph node involvement and all of them were ki67 value >45%. Distance recurrence occurred in 14 pts; 10 of these developed lung metastases. Local recurrence was detected in 5 pts.
Conclusion: TNBC is an aggressive form of breast cancer, which may occur in patients of all ages, but more frequently in younger patients. Our data seem to indicate that in TNBC an anthracyclines-based adjuvant chemotherapy is more effective than regimens without anthracyclines.
Disclosure of Interest: No significant relationships.

P212
EFFECT OF LETROZOLE ON UTERUS WEIGHT AND BONE IN DBA/1 MICE

A. Lintermans[1]*, J. Verhaeghe[2], D. Vanderschueren[2], R. Van Bree[3], J. Vanderhaegen[3], K. Braem[3], R. Lories[3], P. Neven[2]. *[1]Oncology, KU Leuven, Leuven, Belgium, [2]University Hospitals Leuven, Leuven, Belgium, [3]KU Leuven, Leuven, Belgium*

Goals: Ovariectomy (OVX) leads to a rapid decrease in uterus weight and mass as well as both trabecular and cortical bone loss. Here we studied the effects of different dosages of letrozole (LET) on uterus weight and bone parameters in female DBA/1 mice. In parallel we compared these interventions to the effect of fulvestrant (FUL), a selective estrogen receptor down-regulator.
Methods: Thirty-nine female DBA/1 mice underwent OVX (n = 14) or sham operation (n = 25) at 7 weeks of age (= day 0). From day 21 onwards, the OVX group was treated with LET (10 μg/mouse/day; n = 6) or vehicle (n = 8) during 30 days (5 days/week). Sham-operated mice were divided into three groups of 6 mice each and treated with LET (10 μg/mouse/day), high dose LET (200 μg/mouse/day) or FUL (1mg/mouse/day) and one group of 7 control mice. Mice were sacrificed at day 54 and microCT data of femora, uterus and bodyweight and IGF-I levels were assessed.
Results: OVX significantly decreased uterine weights (mean: 8.5mg). The addition of LET slightly but non significantly increased mean uterus weight to 14.2mg. Both groups were significantly different from control animals. Following sham surgery, treatment with LET resulted in a mean uterus weight of 81.1mg and high dose LET in 96.3mg. Mice treated with FUL had a significantly lower mean uterus weight of 64.2mg as compared to LET treated animals, but none of these were significantly different from controls. No differences in baseline or evolution of body weight were seen between all groups. IGF-I levels, measured at moment of sacrifice, were not different between the groups. MicroCT analysis of femora revealed significant trabecular and cortical bone volume loss following OVX relative to sham. However, trabecular bone volume significantly improved following addition of LET in the OVX group. LET or FUL treatment did not affect trabecular or cortical bone volume as compared to controls. However, trabecular thickness was significantly increased in LET or FUL treated animals.
Conclusion: OVX resulted in decreased uterine weights. In addition, as expected, bone loss was observed relative to sham surgery. Remarkably, LET treatment improved bone parameters following OVX.
Disclosure of Interest: No significant relationships.

P213
RECURRENCE SCORE FOR PROGNOSIS AND PREDICTION OF PACLITAXEL BENEFIT IN NODE(+)/ER(+) BREAST CANCER

E.P. Mamounas[1]*, G. Tang[2], S. Paik[2], F.L. Baehner[3], J. Jeong[1], A. Sing[4], S.M. Butler[5], A.P. Sing[4], S. Shak[4], N. Wolmark[1]. *[1]NSABP Operations and Biostatistical Centers, Pittsburgh, United States of America, [2]NSABP, Pittsburgh, United States of America, [3]Pathology, Genomic Health, Inc., Redwood City, United States of America, [4]Pathology, Biostatistics; Medical Affairs, Genomic Health, Inc., Redwood City, United States of America, [5]Pathology, Biostatistics, Genomic Health, Inc., Redwood City, United States of America*

Goals: The Recurrence Score (RS) predicts outcome in ER+ pts treated with adjuvant endocrine therapy (ET) and benefit from adjuvant chemotherapy (CT). We studied the prognostic and predictive impact of RS in N+, ER+ pts treated with adjuvant CT plus ET in the NSABP B-28 trial.
Methods: B-28 compared doxorubicin/cyclophosphamide (ACx4) with AC×4 followed by paclitaxel (PAC)×4. Pts >50 yrs and those <50 yrs with ER+ and/or PR+ tumors also received 5 yrs of tamoxifen concurrently with CT. Between 8/95 and 5/98, 3,060 pts were accrued. Present study includes 1,065 pts ER+ by central TMA IHC, tamoxifen treated, assessed by RS. Median follow-up time was 11.2 yrs.

Table: Kaplan–Meier estimates of 10-yr outcomes

Endpoints	RS Low n = 386	RS Intermediate n = 364	RS High n = 315	Log-rank p-value
LRR %; 95% CI	3.3 (1.8–5.5)	7.2 (4.8–10.3)	12.3 (8.9–16.2)	p < 0.001
DFS event%; 95% CI	24.2 (20.2–28.9)	43.0 (38.1–48.4)	52.0 (46.6–57.7)	p < 0.001
DR %; 95% CI	19.1 (15.4–23.6)	35.1 (30.3–40.4)	44.2 (38.8–50.0)	p < 0.001
Death %; 95% CI	10.0 (7.4–13.6)	25.3 (21.1–30.2)	37.0 (31.8–42.6)	p < 0.001

Results: RS significantly predicted loco-regional recurrence (LRR), disease-free survival (DFS) event, distant recurrence (DR), and death, in univariate analyses (Table). In multivariate analyses, RS was independently prognostic beyond clinical and pathologic factors (p < 0.001). Pts with low RS had similar outcomes when treated with ACàPAC vs. AC (LRR: 3.1% vs. 3.4%, HR = 1.19; DFS event: 23.9% vs. 24.5%, HR = 1.01; DR: 19.1% vs. 19.2%, HR = 0.95; Death 11.5% vs. 8.5%, HR = 1.28, respectively.) Majority of PAC benefit was observed in pts with intermediate RS (LRR: HR = 0.75, DFS event: HR = 0.84, DR: HR = 0.88, death: HR = 0.74) or high RS (LRR: HR = 0.80, DFS event:

HR = 0.81, DR: HR = 0.86, death: HR = 0.86). However, interaction tests between RS and PAC benefit were not statistically significant.
Conclusion: RS significantly predicted risk for LRR, DFS event, DR, and death, in N+, ER+ pts treated with AC or ACàPAC. Although there was no significant interaction between RS and PAC benefit, pts with low RS had similar outcomes whether treated with AC or with ACàPAC and most of PAC benefit was evident in pts with intermediate/high RS. These results support previous findings of lack of CT benefit in pts with low RS.
Support: NCI grants U10-CA-12027, -69651, -37377, -69974, U24-CA-114732, and CA-75362; Susan G. Komen for the Cure® grant; Bristol-Myers Squibb Pharm. Res. Inst.
Disclosure of Interest: As employees at Genomic Health, Inc. (GHI), Drs. Baehner, Butler, Shak, and Sing are compensated with salary, benefits, and stock. They also have stock options as an employees of GHI. Drs. Baehner and Butler also hold <$10,000 of equity in GHI.

P214
COMPARISON OF BONE HEALTH IN CONTINUATION AND STOP GROUPS AFTER 5 YEARS OF ANASTROZOLE: NSAS-BC 05

H. Takei[1] *, H. Ohtsu[2], H. Yagata[3], K. Shimozuma[4], Y. Komoike[5], S. Saji[6], K. Higaki[7], T. Nakamura[8], Y. Ohashi[2], T. Iwase[9]. *[1]Division of Breast Surgery, Saitama Cancer Center, Kita-Adachi, Japan, [2]University of Tokyo, Tokyo, Japan, [3]Breast Surgical Oncology, St. Luke's International Hospital, Tokyo, Japan, [4]Ritsumeikan University, Kyoto, Japan, [5]Kinki University Hospital, Osaka, Japan, [6]Kyoto University Graduate School of Medicine, Kyoto, Japan, [7]Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan, [8]University of Occupational and Environmental Health School of Medicine, Fukuoka, Japan, [9]Cancer Institute Hospital, Tokyo, Japan*

Goals: The National Surgical Adjuvant Study of Breast Cancer (NSAS-BC) 05, a randomized phase III trial was conducted to compare survival between Japanese postmenopausal women with breast cancer who continue to take anastrozole and those who do not, after completing 5 years of adjuvant anastrozole treatment. Bone health was compared as a secondary end point in this trial.
Methods: A total of 165 patients were randomized to enter the continuation group and the same number of patients to enter the stop group. Patient age and body mass index at entry and TNM stage at surgery were the same in the 2 groups. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry. In this study analyses were performed at entry and at 1 year after entry.
Results: The number of patients receiving any treatment for osteoporosis at entry was the same in the 2 groups. The number increased from entry to 1 year in the continuation group and decreased in the stop group; however, no statistical significance was found. The change in BMD from entry to 1 year was not significantly different between the 2 groups when analyzed separately for the presence and absence of bisphosphonate use. Any fractures at any sites were found for 1 year after entry in 1.9% of subjects in the continuation group and 4.4% in the stop group, and no statistically significant differences were found.
Conclusion: Additional adjuvant anastrozole is safe in terms of bone health for 1 year after the completion of 5 years of adjuvant anastrozole in Japanese postmenopausal women with breast cancer.
Disclosure of Interest: No significant relationships.

P215
CARDIAC TOXICITY OF TRASTUZUMAB IN KOREAN WOMEN WHO RECEIVED TRASTUZUMAB AS ADJUVANT THERAPY

C. Cha *, S.G. Ahn, S.A. Lee, H.M. Lee, S.H. Hwang, J. Jeong, H. Lee. *Surgery, Yonsei University Medical College, Seoul, South Korea*

Goals: The age of breast cancer patients in Korea, which is peaked around 50s, differs from that in the West, thus elicits the different pattern of trastuzumab-associated cardiac toxicity. To investigate the clinical presentation of trastuzumab-associated cardiac toxicity in Korean women, we performed this analysis.
Methods: One hundred and twenty-four patients treated in a single institute from January 2006 to November 2011 with adjuvant trastuzumab therapy following primary surgery were identified from database. We evaluated cumulative incidence of cardiac toxicity, associated risk factors and changes of cardiac function during the trastuzumab treatment.
Results: The median age of patients was 50 years (range, 27 to 73). Following up to 12 months, cumulative incidence of cardiac toxicity was 12.1% (Grade I: 8.1%, Grade II: 0.8%, Grade III: 3.2%). During the treatment, 4% of patients were discontinued by the cardiac dysfunction. All of the patients who discontinued or delayed the treatment by the cardiac dysfunction recovered their left ventricular ejection fraction (LVEF) following trastuzumab treatement. The degree of the decrease in LVEF was significantly large at 6 months after initiation of the treatment. Old age than 60 years and high BMI known as risk factors for trastuzuma-associated cardiac toxicity in Western were not demonstrated as significant risk factors in this study. Rather, the low LVEF in baseline was associated with the cardiac toxicity.
Conclusion: The low incidence of the cardiac toxicity and the reversibility of the cardiac dysfunction could validate the safety of the trastuzumab treatment in Korean women with the acceptable level of the baseline LVEF.
Disclosure of Interest: No significant relationships.

P216
COHORT STUDY EVALUATING TRASTUZUMAB IN HER2 POSITIVE EARLY BREAST CANCER IN JAPAN; JBCRG-C01

N. Masuda[1] *, H. Yamashiro[2], H. Iwata[3], R. Nishimura[4], N. Sato[5], T. Kamio[6], T. Saito[7], T. Lee[8], S. Yasuno[9], M. Toi[10]. *[1]Surgery, Breast Oncology, NHO Osaka National Hospital, Osaka, Japan, [2]Breast Surgery, NHO Kure Medical Center and Chugoku Cancer Center, Hiroshima, Japan, [3]Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan, [4]Breast and Endocrine Surgery, Kumamoto City Hospital, Kumamoto, Japan, [5]Surgery, Niigata Cancer Center Hospital, Niigata, Japan, [6]Surgery, Tokyo Women's Medical University Hospital, Tokyo, Japan, [7]Breast Surgery, Saitama Red Cross Hospital, Saitama, Japan, [8]Breast Surgery, Japanese Red Cross Hospital Kyoto Daiichi Hospital, Kyoto, Japan, [9]Kyoto University, Kyoto, Japan, [10]Breast Surgery, Kyoto University Hospital, Kyoto, Japan*

Goals: The past global randomized trials with trastuzumab (H) shows improved outcome in patients (pts) with HER2 positive early breast cancer (BC). However, clinical questions remain including efficacy in elderly and timing to start H therapy. We evaluated the efficacy and safety of H neoadjuvant and adjuvant therapy in an observational study in Japan (UMIN000002737).
Methods: Pts with histopathologically confirmed HER2 positive invasive BC were registered in this cohort study. Eligible pts were female older than 20 years old with stage I-III disease who received H as neoadjuvant and/or adjuvant therapy were eligible.
Results: A total of 2024 pts were registered from 56 institutes between July 2009 and June 2011. Data of 1875 pts were collected and finalized by September 2012. Except 49 cases who have been participating in other clinical trials, except 26 contradiction cases for eligibility-criteria, and then finally 1800 pts' data were analyzed. The median follow-up was 35 months. The mean age was 54.5 years (range: 18–88). The number of elderly pts ≥60 years was 588 (32.7%), cN0 pts was 1039 (57.7%) and estrogen receptor (ER) positive pts was 830 (46.7%), and 752 (90.6%) of them received hormone therapy. Of the 615 pts treated with neoadjuvant chemotherapy (CT), 412 pts (67.0%) received it in combination with H. The number of pts treated with H as adjuvant therapy including

pts treated also in neoadjuvant was 1771 (98.4%): concurrently with CT, 354 pts (20.0%); sequentially following the CT, 766 pts (43.3%); and as H mono-therapy, 631 pts (35.6%). The 3-year disease free survival (DFS) rate was 92.6% (95% CI: 91.0–93.9) and 3-year overall survival rate was 98.2% (95% CI: 97.2–98.8). The 3-year DFS was analyzed for the following subgroups: <60/≥60 years, 94.0%/89.4% (HR = 1.82, p = 0.002); N0/≥N1, 94.8%/89.7% (HR = 2.13, p = 0.0001); ER positive/negative, 93.9%/91.6% (HR = 1.49, p = 0.054); concurrent/sequential CT as adjuvant therapy, 95.4%/94.0% (HR = 1.38, p = 0.356); neoadjuvant/adjuvant CT, 90.8%/94.2% (HR = 1.01, P = 0.962) and CT with anthacycline+taxane/anthracycline only, 95.3%/93.7% (HR = 0.47, p = 0.043). Pts started H as neoadjuvant/adjuvant in combination with CT, 88.5% / 95.2% (HR = 1.97, p = 0.094). No new safety signals were reported.

Conclusion: Results from our study in Japanese HER2 positive BC pts showed treatment in clinical practice was in accordance with the guideline sufficiently, and efficacy of the systemic therapy with H was comparable to data from the past large global trials. Furthermore, timing to start H containing therapies might not affect the outcome.

Disclosure of Interest: No significant relationships.

P217

FERTILITY-PRESERVATION IN BREAST CANCER PATIENTS: AN ITALIAN CONSENSUS

N. Biglia[1] *, F.A. Peccatori[2], M. D'Alonzo[3], M.A. Sarno[4], R. Torrisi[5]. *[1]Gynaecology and Obstetrics, University of Turin Medical School Mauriziano Umberto I Hospital Turin, Turin, Italy, [2]Fertility & Procreation in Oncology Unit Department, Medicine Istituto Europeo di Oncologia, Milan, Italy, [3]Gynaecology and Obstetrics, Mauriziano Umberto I Hospital, Turin, Italy, [4]Istituto Europeo di Oncologia Milan, Milan, Italy, [5]Haematology and Oncology Department, Humanitas Cancer Center Milan, Milan, Italy*

Goals: To achieve agreement on fertility preservation topics among oncologists dealing with breast cancer (BCa).

Methods: 162 panelists were recruited to express anonymously an opinion through a web-platform based on Delphi and. 19 statements were developed from the authors. Each statement was formatted allowing to express a different level of Consensus (1= strong disagreement, 2= moderate disagreement, 3= agreement with high reservation, 4= agreement with minor reservation, 5= strong agreement). The disagreement consensus was declared when >66% of answers where 1+2, whilst the agreement consensus was declared when >66% of answers where 3+4+5.

Results: 91% of oncologists consider important to discuss with patients about fertility issues and 81% is contrary to cryopreservation of embryos. Regarding the ovarian stimulation, 37% fear a delay in starting chemotherapy and 83% believe estrogens could stimulate the growth of hidden cancer cells mostly in ER+ve tumors. Difficulties in accessing to fertility preservation procedures depend on the reluctance of patients, but 90% of panel members underline also lack of coordination with medically assisted procreation center. No full consensus was reached on the prognostic role of pregnancy after BCa 54% of oncologists declared that pregnancy does not affect oncologic prognosis and that is safe for either mother and fetus (60%). 56% of oncologists recognized a potential negative role of ovarian stimulation in BCa patients with BRCA mutation. Nonetheless, 62% of oncologists reported no contraindications to natural pregnancy in BRCA mutation carriers. Agreement consensus was reached on breastfeeding in breast cancer patients (91%), also from one breast only in patient underwent mastectomy (70%). Regarding the choice of adjuvant systemic therapy, 68% and 83% of panelists do not omit alkylating agents or consider shorter regimens, respectively and 76% do not shorten tamoxifen duration. The use of GnRHa during chemotherapy is considered as the only medical means for preserving ovarian function: for 90% of panelists literature data are convincing and 79% declare to use it regularly. 68% of panellists propose GnRHa for 5 yrs in pts with ER+ve tumors, particularly in young women (79%) and at high risk of relapse (83%). Finally, 66% of panelists consider positively the occurrence of early menopause in women with ER+ve tumors.

Conclusion: Fertility preservation in breast cancer patients is a well accepted practice among italian oncologists. A good agreement has been observed on the majority of the issues.

Disclosure of Interest: The authors: N.B., F.P., R.T. are members of an advisory board for Ipsen Spa

P218

COMPARISON OF PATIENT-REPORTED OUTCOMES BETWEEN THE CONTINUATION AND STOP GROUPS AFTER 5 YEARS OF ANASTROZOLE: NSAS-BC 05

H. Yagata[1] *, H. Ohtsu[2], K. Shimozuma[3], Y. Ohashi[2], Y. Komoike[4], S. Saji[5], H. Takei[6], T. Nakamura[7], T. Iwase[8]. *[1]Department of Breast Surgical Oncology, St. Lukes's International Hospital, Tokyo, Japan, [2]University of Tokyo, Tokyo, Japan, [3]Ritsumeikan University, Kyoto, Japan, [4]Kinki University Hospital, Osaka, Japan, [5]Kyoto University Graduate School of Medicine, Kyoto, Japan, [6]Saitama Cancer Center, Saitama, Japan, [7]Orthopedics, University of Occupational and Environmental Health School of Medicine, Fukuoka, Japan, [8]Cancer Institute Hospital, Tokyo, Japan*

Goals: To compare the change in patient-reported outcomes (PROs) between the continuation and stop groups after completing 5 years of anastrozole-based adjuvant endocrine therapy in the NSAS-BC 05 trial, a randomized clinical trial designed to assess the efficacy of an additional 5 years of anastrozole in postmenopausal women with breast cancer.

Methods: Patients registered in NSAS-BC 05 were asked to fill in several validated health-related quality of life (HRQOL) instruments, including the SF-36 and sub-scale of the Functional Assessment of Cancer Therapy-Endocrine Symptoms (FACT-ES), at baseline and at 1 year.

Results: HRQOL at baseline and 1 year were collected from 290 patients at 64 institutions in Japan. Mean age was 64 years, and body mass index was less than 25 in 75.5% of the patients. In the SF-36 scale profiles, role-physical (RP), vitality (VT), role-emotional (RE), and mental health (MH) showed slight decreases in both groups, physical functioning (PF) and bodily pain (BP) in the continuation group, and social functioning (SF) in the stop group. No differences were seen between the groups in any changes of the scores. The sub-scale score of FACT-ES showed a slight decrease only in the stop group, but there was no significant difference between the groups in the change or the scores.

Conclusion: After 5 years of anastrozole administration, its continuation did not have an adverse impact on HRQOL compared with stop as assessed at 1 year. We plan to assess HRQOL annually until after 6 years.

Disclosure of Interest: No significant relationships.

P219

THE 2006 ADJUVANT TRASTUZUMAB CONVENTION IN BELGIUM: 5 YEARS LATER

J. Vanderhaegen[1] *, R. Paridaens[1], A. Lintermans[2], O. Brouckaert[1], P. Neven[1]. *[1]Multidisciplinary Breast Center, Catholic University Leuven, Leuven, Belgium, [2]Oncology, KU Leuven, Leuven, Belgium*

Goals: A year prior to its reimbursement (June 1st 2007), the Belgian health authorities offered adjuvant trastuzumab to women with a HER-2 amplified breast cancer. Since long term follow-up data from large series of women treated with adjuvant trastuzumab outside clinical trials are lacking, we here report 5 year follow-up data of patients receiving adjuvant trastuzumab for one year within this 'Trastuzumab Convention'.

Methods: Demographics, histopathologic features, baseline (≥55%) and follow-up left ventricular ejection fraction (LVEF) together with 5 yr breast cancer related events (BCRE) were centrally recorded. Outcome was reported by grade, lymph node (pN) status, hormone receptor (HR) status, timing of CT (neo-or adjuvant) and duration of trastuzumab treatment (≤1 year).
Results: 917 patients (pts) were included. To date, files on histopathology, demographics, LVEF and therapy are available for 887 (97%) pts, outcome for 738 (80%). Median age at diagnosis was 53 years (25–81); 56% of tumors were >pT1, 57% pN+, 72% grade 3, 59% HR-positive for estrogen receptor (ER) and/or progesterone receptor (PR). 20% of pts had neo-adjuvant and 80% adjuvant CT; 86% radiotherapy and 50% endocrine therapy. Median follow-up was 63 (range 8–90) months. Premature (<1 year) treatment discontinuation occurred in 17% of pts mainly because of decrease in LVEF (asymptomatic in 7.2%). A BCRE appeared in 128 pts (17%) on average 31 months (range 4–76) after diagnosis. BCRE was metastatic in 96 pts (13%) and mostly (71%) limited to one organ at diagnosis, with preference for liver (18%), lung (17%), brain (16%) and bone (13%). 7% of patients died of breast cancer. Distant BCRE occurrence was more frequent in pts receiving neo-adjuvant (24%) versus adjuvant CT (10%) and was further affected by lymph node involvement, grade 3, negative HR and negative PR in ER-positive disease. For the conference, updated data will be presented with emphasis on cardiac function and the effect of premature treatment discontinuation on patients' outcome.
Conclusion: Outside a clinical trial, >80% of patients eligible for adjuvant trastuzumab is able to complete treatment. Outcome at 5 years is favourable with low symptomatic cardiac toxicity and a 13% incidence of metastatic relapse, being lowest in pN−, <grade 3, HR+ and ER+/PR+ tumors. Updated outcome will be presented at the conference.
Disclosure of Interest: No significant relationships.

P220
EVEROLIMUS PLUS ADJUVANT ENDOCRINE THERAPY IN HIGH RISK BREAST CANCER: THE UNIRAD STUDY

F. André[1] *, S. Chabaud[2], A. Martin[3], J. Lemonnier[3], T. Bachelot[2], M. Campone[4]. *[1]Institut Gustave Roussy, Institut Gustave Roussy, Villejuif, France, [2]Centre Léon Bérard, Lyon, France, [3]R&D UNICANCER, Paris, France, [4]Institut de Cancérologie de l'Ouest – René Gauducheau, Centre de Recherche en Cancérologie, Nantes Saint Herblain, France*

Goals: Although progress has been made in the adjuvant treatment of breast cancer, patients with higher-risk disease (ie, >3N+ and/or T3/4) will relapse after adjuvant therapy. Everolimus (EVE) is an oral mammalian target of rapamycin (mTOR) inhibitor that has shown clinical activity with exemestane in the advanced breast cancer setting (BOLERO-2; postmenopausal women with hormone-receptor-positive, human epidermal growth factor receptor-2-negative [HER2−] disease, progressing after prior letrozole or anastrozole). Administration of EVE earlier during adjuvant therapy may decrease the relapse rate, especially in patients with high nodal involvement and/or persistent nodal involvement after neoadjuvant therapy. In this setting, the UNIRAD study is examining disease-free survival (DFS) after addition of EVE to adjuvant therapy during the last 2 years of treatment.
Methods: UNIRAD is a multicenter, randomized, double-blind, phase 3 study in women with nodal involvement (≥4 if initial therapy and ≥1 after neoadjuvant therapy), no metastases, and estrogen-receptor-positive (ER+) and HER2− breast cancer who remain disease free after receiving 3 years of adjuvant hormone therapy. Patients will be randomized to receive the combination of EVE (10 mg/day) + ongoing endocrine therapy versus placebo + ongoing endocrine therapy for 2 years to complete 5 years of adjuvant endocrine therapy. Randomization is stratified by center, endocrine therapy (tamoxifen or aromatase inhibitors), previous adjuvant versus neoadjuvant therapy, and age (≤70 vs >70 years). Follow-up will continue for 5 years after treatment. The primary endpoint is DFS for EVE versus placebo. Secondary endpoints include overall survival, event-free survival, distant metastasis-free survival, DFS and OS in hormone subgroups, safety, incidence of secondary cancers, quality of life, and predictive value of mTOR activation markers on DFS.
Results: UNIRAD opened for enrollment in January 2013, with an estimated population of 1,984 women.
Conclusion: This study will provide efficacy and safety information on EVE + adjuvant therapy versus adjuvant therapy alone in patients with high-risk ER+ HER2− breast cancer.
Disclosure of Interest: André: Financial support from Sanofi-Aventis, Novartis, Roche, and AstraZeneca. Chabaud, Martin and Lemonnier: Nothing to disclose. Bachelot: Received research support from Novartis. Campone: Consultant for Novartis and Servier.

P221
Abstract withdrawn

P222
Abstract withdrawn

P223
MAMMAPRINT® PRESCREEN ALGORITHM (MPA) REDUCES CHEMOTHERAPY IN SOUTH AFRICAN BREAST CANCER PATIENTS

K.A. Grant[1] *, J. Apffelstaedt[2], C. Wright[3], E. Myburg[4], R. Pienaar[5], M. De Klerk[6], M. Kotze[7]. *[1]Biomedical Sciences, Cape Peninsula University of Technology, Cape Town, South Africa, [2]Department of Surgery, University of Stellenbosch, Cape Town, South Africa, [3]Department of Pathology, Tygerberg Hospital, Cape Town, South Africa, [4]Panorama Medi-Clinic, Cape Town, South Africa, [5]Panorama Medi Clinic, Cape Town, South Africa, [6]Metropolitan Health Group and Business School of the University of Stellenbosch, Cape Town, South Africa, [7]Anatomical Pathology, University of Stellenbosch, Cape Town, South Africa*

Goals: Molecular predictors of outcome and drug sensitivity have the potential to reduce the indiscriminate chemotherapeutic use in patients who have an almost insignificant risk of relapse. This prompted a South African medical insurer to subject the 70-gene MammaPrint® (MP) test to a health technology assessment (HTA) in 2009. The HTA introduced a set of test eligibility criteria – the MammaPrint® Prescreen Algorithm (MPA). The goal of this study was to evaluate the clinical usefulness of the MPA using a comprehensive computer-based clinical decision support system known as the Pathology Supported Genetic Testing (PSGT) service.
Methods: The study population consisted of 91 early-stage South African breast cancer patients referred for the MP test, of which 56 were fresh biopsies and 35 from FFPE sections.
Results: When applying the HTA-derived MPA for determination of MP testing eligibility, 84 of the 91 patients enrolled in the study qualified. Sixty-four percent (54/84) of patients in this subgroup were classified as low risk using the MP test.
Conclusion: The MP test classifies approximately 40% of early-stage breast cancer patients as low-risk compared to 15% using conventional criteria, while application of the MPA identified more than 60% of patients subjected to the MP test as low risk. Assessment of clinico-pathological risk factors in conjunction with the MP test is an appropriate strategy to prevent overtreatment in early stage breast cancer.
Disclosure of Interest: No significant relationships.

P224

ADJUVANT CHEMOTHERAPY AND DISEASE OUTCOME IN TRIPLE-NEGATIVE BREAST CANCER: 3-YEAR FOLLOW-UP DATA

S. Susnjar[1] *, V. Posarac[2], Z. Milovanovic[3], M. Milovic-Kovacevic[1], L. Stamatovic[1], D. Gavrilovic[4], A. Karaferic[1]. [1]*Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [2]*Department of Surgical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [3]*Department of Pathology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [4]*Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

Goals: To evaluate the association of type of adjuvant chemotherapy (ACT) and disease outcome in triple-negative breast cancer (TNBC) patients (pts).

Methods: We identified a group of 239 stages I–IIIB TNBC pts diagnosed from 2006 and 2009 at our institution. TNBC status was defined as IHC ER 0–3/PR 0–3/HER2:0–1,2/CISH–. All of them were treated with radical surgery ± (neo-N) ACT ± adjuvant radiotherapy, as per protocol. The association of age, menopausal status, tumor histology, size and grade, nodal status, HR/HER2 phenotype (ER0/PR0/HER2:0 vs. non-ER0/PR0/HER2:0) and disease outcome were also analyzed. The main end points were disease-free survival (DFS) and overall survival (OS). Statistics included Kruskal–Wallis Test, Wilcoxon rank sum test, Pearson Chi-squared test, Kaplan–Meier survival analysis and Log-rank test.

Results: Median age was 56 years (range 26–84), 30% being premenopausal. They were followed for a median of 39 mos (range 2–78). Fifteen pts received NACT (4–6 FA(E)C cycles), followed by A-FA(E)C (6/15) or A-taxanes (6/15). In total, 192 (80%) pts received ACT: 64 (27%) CMF, 100 (42%) FA(E)C and 28 (12%) combination of anthracyclines and taxanes (AT). Older women were more likely to be treated with no therapy or CMF compared to women receiving FA(E)C or AT therapy (Kruskal–Wallis Test, $p = 0$). Significantly higher number of pts treated with AT had node positive (N+) disease compared to pts with no therapy or CMF or FA(EC) (Pearson Chi-squared test, $p < 0.001$) and had more involved nodes, as well (Kruskal–Wallis Test $p = 0.00003$). Among N+ pts (92/239) there were no difference in the number of positive nodes between subgroups divided according to ACT (Kruskal–Wallis Test, $p = 0.055$). In total, 53 (22%) pts developed disease relapse. Significantly higher proportion of pts treated with AT developed disease relapse compared to CMF (Pearson Chi-squared Test, $p = 0.04$) and FA(E)C subgroups (Pearson Chi-squared Test, $p = 0.03$), on the account of pts with bone lesions (Fisher Exact Test: $p = 0.003$). There was statistically significant difference in DFS between treatment subgroups (Log-Rank test, $p = 0.046$), being significantly reduced in AT compared to CMF (Log-Rank test, $p = 0.007$) and FA(E)C subgroups (Log-Rank test, $p = 0.005$). However, there was no difference in OS between treatment subgroups.

Conclusion: It seems that there was no apparent difference in disease outcome between treatment subgroups in TNBC pts during short follow-up period. This might be explained by low number of events and low number of pts treated with AT therapy, which was introduced as routine therapy in the mid of 2009.

Disclosure of Interest: No significant relationships.

Radiotherapy/IORT

P225

DOSIMETRIC STUDY COMPARING PHOTON AND ELECTRON BEAMS FOR BOOSTING THE TUMOR BED IN BREAST CANCER

S. Ahmed[1], M. Mahmoud[2] *, E. Attalla[1], H. Abouelenein[1], M. Barsoum[2]. [1]*Radiotherapy Department, Children's Cancer Hospital Egypt, Cairo, Egypt,* [2]*Radiotherapy, National Cancer Institute Egypt, Cairo, Egypt*

Goals: To assess and compare the potential dosimetric advantages and drawbacks of photon beams and electron beams as a boost for the tumor bed in superficial and deep seated early-stage breast cancer.

Methods: Planning CTs of 10 women with early breast cancer underwent breast conservative surgery were selected. Tumor bed was defined as superficial and deep with a cut of point 4 cm, those with less than 4 cm were defined as superficial tumors representing 4 patients and those with depth of 4 cm or more were classified as deep tumors representing 6 patients. The clinical target volume (CTV) was defined as the area of architectural distortion surrounded by surgical clips. The planning target volume (PTV) was the CTV plus margin 1 cm. A dose of 10 Gy in 2 Gy fractions was given concurrently at the last week of treatment. Organs at risk (OARs) were heart, lungs, contra-lateral breast and a 5-mm thick skin segment of the breast surface. Dose volume histograms were defined to quantify the quality of concurrent treatment plans assessing target coverage and sparing OARs. The following treatment techniques were assessed: photon beam with 3D-conformal technique and a single electron beam.

Results: For superficial tumors better coverage for CTV and PTV with good homogeneity with better CI was found for the 3DCRT but with no significant planning objectives over electron beam. For deep tumors, the 3DCRT met the planning objectives for CTV, PTV with better coverage and fewer hot spots with better homogeneity and CI. For superficial tumors, OARs were spared by both techniques with better sparing for the electron beam where as for deep tumors also OARs were well spared by both techniques.

Conclusion: Boosting the tumor bed in early-stage breast cancer with optimized photon may be preferred to electron beam for both superficial and deep tumors. The OARs dose sparing effect may allow for a potential long-term toxicity risk reduction and better cosmesis.

Disclosure of Interest: No significant relationships.

P226

INTRAOPERATIVE RADIOTHERAPY IN EARLY BREAST CANCER – LONG TERM FOLLOW UP

M. Steiner *, A. Biterman, E. Shiloni, M. Leviov, A. Kremer, R. Hanna, J. Goldman. *Oncology, Carmel Medical Center, Haifa, Israel*

Goals: From 2006 we introduced intraoperative radiotherapy as the only post lumpectomy breast irradiation in low risk early breast cancer patients. Treatment was offered as an alternative to the standard post-operative whole breast external irradiation to patients with invasive ductal carcinoma older than 60 years with clinical tumors up to two cm and clinically negative axillary nodes. It was offered too to younger patients or patients with other histology and tumors up to 4 cm if they were not candidate for standard radical therapy.

Methods: Soft Xray irradiation (50 KV) generated by Intrabeam System was used giving 20 Gy at the surface of surgical cavity. This results in 6–7 Gy at one cm depth.

Results: Up to day 380 patients were treated. We report the long term results of the first 100 patients treated during 9/2006–2/2009. Their median age was 70 years (56–87). Median clinical tumor size (as measured by US) was 13 mm (5–30). 24 patients had mild to moderate local complications: 7 wound infection, 12 seromas (10 of them complicated) and 5 local bleeding or hematoma. 8 patients experienced major complications: 3 delayed healing (>90 days), 2 required surgical intervention, one hospitalization for IV antibiotics, one small skin necrosis and one RTOG grade III fibrosis. At final pathology, median tumor size was 14 mm (1–32). Pathologic free margins >1 mm were found in 98 patients and >2 mm in 94. 18 patients were found to have axillary l-nodes involved in 16 of them only one node. 5 patients had additional local therapy (one mastectomy and 4 whole breast irradiation) due to unexpected adverse pathologic findings. During median follow up of 51 months (40–73), four ipsilateral breast failures were observed: two new primaries (by location and histology) and two true local failures.

Two were treated by lumpectomy and breast irradiation and two by mastectomy One patient developed contralateral breast cancer and one had systemic disease without local failure.

Conclusion: We conclude that long term follow up suggests that intraoperative radiotherapy using the Intrabeam system is feasible and may offer a convenient alternative to post operative external whole breast irradiation in selected low risk early breast cancer patients. Most complications are mild or moderate and self limiting. Longer follow up on larger series of patients is still needed to evaluate final results and late toxicity.

Disclosure of Interest: No significant relationships.

P227

TWO DOSE FRACTIONATION SCHEDULES OF RADIATION IN POSTMASTECTOMY BREAST CANCER PATIENTS

P. Kumbhaj*, O.P. Sharma, R. Sharma, A.R. Bhatnagar. *Radiotherapy, SMS Medical College Jaipur, Jaipur, India*

Goals: To compare the two different dose fractionation schedules in terms of overall treatment, locoregional control, acute and late toxicities, and patient compliance.

Materials and Methods: Patients of postmastectomy non metastatic breast cancer were randomized in two arms: arm A (44), Arm B (45) according to dose fractionation schedule of external radiation given to chest wall and draining lymphatics. Arm A was given 50 Gy in 25 fractions in 5 weeks and Arm B was given 40 Gy in 17 fractions in 3.2 weeks. After completion of radiation patients were kept on regular follow up.

Results: Median follow up was 21 months. In arms A & B the median overall treatment time was 41 and 28 days with respective ranges of 35–46 days and 21–32 days. The patients in both the arms tolerated radiation well, skin reactions were most common. Grade II and III acute reactions were comparable in both arms. There was non significant increase in both late skin and subcutaneous skin toxicities in arm B. Result of treatment of both arms are as follows chest wall failure 6% v/s 8% ($p > 0.05$), nodal failure 9% v/s 8% ($p > 0.05$), distant mets 26% v/s 29% ($p > 0.05$).

Conclusion: Both the studied dose fractionation schedules (A) 50 Gy/25 fractions/5 weeks & (B) 40 Gy/17 fractions/3.2 weeks are equally efficacious in terms of locoregional control, acute and late toxicities. The shorter schedules in Arm B gives an added advantage of decreased overall treatment time, which in turn can result in better patient compliance and decrease the work load of overburdened department.

Disclosure of Interest: No significant relationships.

P228

VERIFICATION OF IN-FIELD DOSE AND CONTRALATERAL BREAST DOSE IN POST-MASTECTOMY RADIOTHERAPY

N. Sesikeran[1]*, M.I. Malik[2], N. Jagannathrao[2], S. Pamidighantam[2]. [1]*Radiation Oncology, Apollo Cancer Hospitals, Hyderabad, India,* [2]*Radiation Oncology, Nizams Institue of Medical Sciences, Hyderabad, India*

Goals:

- To estimate the actual dose received by surface within the treatment field and to compare it with point dose as estimated by the ECLIPSE planning system.
- To quantify the effect of adding a 0.5 cm bolus material to the surface dose.
- To quantify the dose received by the contralateral breast.
- Dose Volume Histogram analysis for organs at risk.

Methods: 20 female patients requiring post mastectomy radiotherapy were included in the study. Patients were immobilized in a thermoplastic mould and simulation was done using spiral CT scan with 5 mm thick slices. Images were transferred to eclipse planning system and 3DCRT plans were generated with virtual bolus for first 13 fractions. Planned dose was measured at fixed points on the surface i.e In-field dose was measured at a point 8 cm from the medial tangential field edge at the mid-plane of the chest wall field and contralateral breast dose was measured at a point 5 cm from the medial tangential field edge. Doses at corresponding points over the surface are measured during treatment using semiconductor diode detectors (scanditronix 3G-pSi diodes). Two readings are taken with bolus (superflab 0.5 cm thick) and two readings without bolus. Electrometer readings were taken at the end of each field and analyzed. Data analysis was done using Windows SPSS software for Statistical analysis.

Results: Variation of delivered dose from planned dose, as measured by semiconductor diodes was found to be within a range of −12% to 7.9% for fractions with bolus with a mean variation of 1.5% ($p = 0.2$). Variation of delivered dose from planned dose, for fractions without bolus was within a range of −7.6% to 11%, with a mean variation of 4.3% ($p = 0.001$). Planning system underestimated the surface dose in the absecnce of bolus. Mean dose difference at the surface provided by adding bolus was 0.05 Gy ($p = 0.2$). Mean dose received by the contralateral breast 2.23 Gy (4.45% of prescribed dose). Contribution of medial tangential field to CLB dose was significantly more compared to the other fields ($p = 0.01$). Mean dose to lung, heart, spinal cord and oesophagus were within tolerance limits. Increase in wedge angle was associated with significant increase in lung dose and contralateral breast dose.

Conclusion: Dose contribution to contralateral breast and lung using 3DCRT was mainly from the medial tangential wedged field and hence can be further decreased by reducing the wedge angle or avoiding its use. Use of 0.5 cm bolus material did not result in significant increase in surface dose to the chest wall. Despite several uncertainties in day to day treatment such as daily setup variation and respiratory motion of chest wall, reasonably accurate delivery of radiation was found, as measured by silicon diode detectors.

Disclosure of Interest: No significant relationships.

P229

HIGH DOSE RATE BRACHYTHERAPY VERSUS ELECTRON BEAM BOOST IN TREATMENT OF EARLY BREAST CANCER

C. Singh[1]*, R. Sharma[2], O.P. Sharma[2]. [1]*Department of Radiotherapy and Clinical Oncology, S.M.S. Medical College and Hospital, Jaipur, Rajasthan, India,* [2]*Radiotherapy, SMS Medical College Jaipur, Jaipur, India*

Goals: To evaluate the effect of high dose rate brachytherapy (HDR BT) versus electron beam boost on local tumor control, side effects and cosmesis after breast conserving surgery in early breast cancer.

Methods: 60 women with stage I-II breast cancer who underwent breast conserving surgery were treated with 50 Gy adjuvant radiotherapy to the whole breast and then randomly assigned to receive 15–16 Gy boost to the primary tumor bed either with HDR BT ($n = 30$) or electron boost ($n = 30$) using linear accelerator. HDR BT was performed using Iridium-192 temporary implants. Breast cancer related events, side effects and cosmetic results were assesed after one year.

Results: No significant difference in local tumor control was found in patients treated with HDR BT or electron boost. However, cosmesis was better in patients receiving electron boost than those receiving HDR BT. HDR BT was associated with increased fibrosis and pigmentation.

Conclusion: Electron boost provides better cosmesis and lesser fibrosis than HDR BT in patients of early breast cancer undergoing breast conserving surgery. However, long term follow up studies are needed for locol tumor control assesment. Breast conserving surgery is preferred because of better psychosexual quality of life.

Disclosure of Interest: No significant relationships.

P230

TARGETING HSP90 CHAPERONE ACTIVITY IN HUMAN BREAST CANCER CELLS CAN SENSITIZE THEM TO RADIOTHERAPY

V. Kudryavtsev*, A. Demidkina, V. Mosina, A. Kabakov. *Department of Radiation Oncology, Medical Radiology Research Center, Obninsk, Russian Federation*

Goals: Irradiation is often used as a pre-operative procedure in primary therapy of breast tumors, while their cells are rather radioresistant. Therefore, there is a need of selective radiosensitizers for more effective killing these malignant cells. Our study was aimed at examining effects of an inhibitor of the heat shock protein 90 (Hsp90) chaperone activity, 17AAG, on the radiation response of breast cancer cells.

Methods: MCF-7 cell cultures derived from human breast carcinoma were exposed to clinically relevant doses (2–5 Gy) of gamma-rays, while some cell samples were co-treated with 10–500 nM 17AAG. Inhibition of the cellular Hsp90 chaperone activity was detected on a delay in the Hsp90-mediated reactivation of thermally denatured luciferase in the heat-stressed transfectants. The cell death/survival was assessed in TUNEL, annexin-V staining and clonogenic assays. The expression of cell death/survival-, DNA repair- and angiogenesis-related proteins were probed by immunoblotting. The p53 and ATM patterns were visualized by immunofluorescence.

Results: In the breast cancer cells, low (40–150 nM) concentrations of 17AAG inhibited the Hsp90 chaperone function and down-regulated the Akt, survivin, HIF-1alpha, VEGF and Bcl-2 levels; also, the irradiation-responsive phosphorylation of Akt and its down-stream targets such as Bad, XIAP, GSK-3 or MDM2 became impaired. Enhanced activation of p53 and its longer up-regulation along with the inhibition of phosphorylation and nuclear translocation of ATM were found in the cells irradiated at 2–5 Gy after incubation with 40–150 nM 17AAG. These cell samples exhibited massive apoptosis and sharply decreased clonogenic ability (DEFs: 1.5–1.9), whereas the same radiation doses without 17AAG induced the less cytotoxicity and only a slight decrease in the clonogenicity. The 17AAG-conferred radiosensitization seems to be due to down-regulation or inactivation of antiapoptotic proteins (Akt, Bcl-2, survivin, XIAP), activation of pro-apoptotic proteins (Bad, GSK-3) and switching the MDM2/p53/ATM-mediated DNA damage response from cell survival to cell death. Besides, 50–200 nM 17AAG impaired the angiogenic potential of MCF-7 cells by down-regulating the HIF-1alpha and VEGF expression in them.

Conclusion: Clinically achievable concentrations of 17AAG enable to improve the radiation-induced elimination of breast tumor cells and suppress the tumor-stimulated angiogenesis. Therefore, pharmacological inhibitors of the Hsp90 activity may be used in primary therapy of breast cancer.

Disclosure of Interest: No significant relationships.

P231

TARGIT-A TRIAL (TARGETED INTRAOPERATIVE RADIOTHERAPY): UPDATED ANALYSIS OF LOCAL RECURRENCE

M. Baum*, on behalf of the TARGIT Trialists Group. *Ucl Division of Surgery, Clinical Trials Group, London, United Kingdom*

Goals: TARGIT-A, a non-inferiority randomised controlled trial (ISCRTN 34086741, Lancet 2010; 376: 91–102) compared outcomes in patients undergoing breast conserving surgery followed by a risk-adaptive approach using a single dose of targeted intra-operative radiotherapy (TARGIT) or whole-breast external beam radiotherapy (EBRT) over several weeks. The primary endpoint was local recurrence in the conserved breast.

Methods: Randomisation was to TARGIT or EBRT in a 1:1 ratio. If allocated to TARGIT, patients in whom adverse risk factors were discovered on the final pathology report could receive EBRT (the risk-adapted approach). Patients allocated to receive EBRT received conventional whole-breast radiotherapy according to local practice. The primary outcome was ipsilateral within breast recurrence (IBR) with an absolute non-inferiority margin of 2.5% at 5 years. Secondary outcomes included survival and local toxicity/morbidity. Exploratory analyses included loco-regional recurrence, 'all recurrence' (ipsilateral or contralateral breast, axilla or distant), distant recurrence, and cause of death.

Results: In total, 3451 women were randomised from 33 centres in 10 countries between 2000 and 2012. Median follow-up of the whole cohort was 2 years 5 months. 2020 patients have a median 4 y follow up and 1222 patients have median 5 y follow up. For the primary outcome of ipsilateral breast recurrence, the absolute difference at 5-years was 2.01% (0.32 to 3.7%), which was higher with TARGIT but was within the pre-specified non-inferiority margin of 2.5% (Table 1). For the secondary outcomes, there was a non-significant trend for improved overall survival with TARGIT [HR = 0.70 (0.46–1.07)] due to fewer non-breast cancer deaths [17 vs. 35, HR 0.47 (0.26–0.84)].

Table 1: Primary and secondary analyses (5 y cumulative risk (95% CI)

	TARGIT (n = 1721)	EBRT (n = 1730)	HR (95% CI)
IBR	3.3% (2.1–5.1%)	1.3% (0.7–2.5%)	2.1 (1.0–4.3)
All recurrence	8.2% (6.3–10.6%)	5.7% (4.1–7.8%)	1.5 (1.0–2.1)
Death	3.9% (2.7–5.8%)	5.3% (3.9–7.3%)	0.7 (0.5–1.1)

IBR = In Breast Recurrence in the conserved breast.

Conclusion: The risk-adapted approach of TARGIT, using a single dose of radiotherapy at the time of surgery (with the option of adding EBRT if required) is non-inferior to conventional EBRT for the primary endpoint of IBR. There was no difference in overall survival, but a non significant trend favouring TARGIT.

Disclosure of Interest: Carl Zeiss provides support for ISC meetings, consultancy and honorarium.

P232

HYPOFRACTIONATED WHOLE BREAST RADIATION IN EARLY BREAST CANCER: A FEASIBILITY REPORT

S. Kakkar*, V.A.R. Palkonda, K. Bhattacharya, N. More, S. Das, P. Upadhyaya, S.N.S. Reddy. *Radiation Oncology, Apollo Cancer Hospitals, Hyderabad, India*

Goals: To assess the feasibility, acute and late toxicities and loco-regional control with Hypofractionated whole breast radiotherapy in early breast cancer patients in Indian population.

Methods: This is an ongoing Phase II open label study where women with operable, invasive early breast cancer (pT1–2 N0–1 M0), post Breast Conservation Surgery and chemotherapy were eligible for inclusion after necessary approval from Institutional Review Board and Ethics Committee. 25 patients were accrued between February 2011 and August 2012 and analysed in the present study. All the patients were treated with either IGRT or Rapid Arc SIB technique in Novalis Tx machine. The dose fractionation scheme to Whole Breast was 4320cGy in 16 fractions, 270cGy/fraction, and Tumor Bed Boost 4800cGy in 16 fractions, 300cGy/fraction. The toxicities were assessed every week during radiotherapy, at Ist, 3rd month and each follow-up as per RTOG Toxicity Criteria. Cosmesis was graded as per Harvard Criteria at every follow-up.

Results: With a minimum follow-up of 3 months (3–21 months), 25 patients were included in the present analysis. The mean age of patients was 53years. 5/25 (20%) and 20/25 (80%) patients had pT1, pT2 lesions respectively. 18 (72%) and 7 (28%) patients had N0, N1 disease respectively. The acute skin toxicity was Grade 0: 13/25 (52%), Grade 1: 10/25 (40%) and Grade 2: 2/25 (8%). None of the patients had Grade 3 or 4 toxicities. 17/25 (68%), 8/25 (32%) patients had excellent and good cosmesis respectively. 10/25 (40%) patients had mild pain (1/10 as per Visual Analog Pain scale) in the breast,

15 (60%) had no acute pain during radiotherapy. No local failures were observed during follow-up.

Conclusion: The hypofractionated whole breast radiotherapy protocol was very well tolerated with no Grade3/4 acute skin toxicity and Excellent to Good cosmesis at follow-up. More mature and long term follow-up is required to assess clinical outcomes and late toxicities.

Disclosure of Interest: No significant relationships.

P233

IDENTIFYING A SENSITIVITY PREDICTION PROFILE FOR PATIENTS UNDER ADJUVANT TREATMENT FOR BREAST CANCER

A. Gounaris[1] *, X. Provatopoulou[1], E. Kalogera[1], M. Piperi[2], P. Grigoropoulos[3], E. Athanasiou[2], G. Zografos[4]. *[1]Research Center, Hellenic Anticancer Institute, Athens, Greece, [2]Radiation Oncology Department, General Oncological Hospital of Kifissia "Ag. Anargiroi", Athens, Greece, [3]1st Surgical Ward, AGII Anargyroi General and Oncological Hospital, Nea Makri, Greece, [4]1st Department of Propaedeutic Surgery, Hippocrateion Hospital, Athens Medical School, University of Athens, Athens, Greece*

Goals: Although the beneficial effect of radiation therapy on breast cancer progression is well documented, RT administration is often accompanied by complications. Among significant irradiation sequel, lung tissue injury and inflammation emerges as a critical one. Due to the high lifetime risk of breast cancer patients, it is of uttermost interest to identify the parameters that could contribute to the prediction of lung injury and the designing of a tailored treatment. The objective of the study was to investigate the potential role of circulating biomarkers in the prediction of therapy-induced pulmonary complications.

Methods: The study included 38 patients with primary breast cancer under postoperative radiation therapy and 30 healthy controls. Patients were monitored for a study period of three months. Peripheral blood samples were collected at selected time-points: prior to the initiation, during and at completion of RT, as well as during a two-month follow-up period. Circulating levels of CRP, YKL-40 and SP-D were quantitatively determined using enzyme linked immunosorbent assay. Soluble expression of ICAM-1, sRAGE, TNFRI and TNFRII was measured by Luminex xMAP technology.

Results: Pre-radiotherapy levels of CRP, SP-D and sRAGE were significantly higher in patients compared to healthy controls ($p < 0.001$, $p < 0.05$ and $p < 0.05$, respectively). CRP, SP-D and YKL-40 levels exhibited a gradual increase after the initiation of RT and during follow-up, however only the rate of change in SP-D levels was significant ($p < 0.005$). ICAM-1 and TNFRII levels exhibited a non-significant decrease during the study period, while TNFRI and sRAGE expression remained approximately stable.

Conclusion: Our observation of significantly higher pre-radiotherapy circulating levels of CRP, SP-D and sRAGE suggests that breast cancer patients exhibit a profile of lung tissue injury and inflammation even before the administration of RT, potentially attributed to prior therapeutic management. Gradually increasing levels of CRP, SP-D and YKL-40 indicate a further induction of pulmonary complications as an effect of irradiation. In the absence of clinical and imaging findings, our data support that SP-D and potentially CRP can provide useful biomarkers for the early detection of therapy-induced pulmonary complications before the onset of clinical evidence.

Disclosure of Interest: No significant relationships.

P234

OMITTING WHOLE BREAST RADIOTHERAPY DOES NOT INCREASE AXILLARY RECURRENCE – DATA FROM TARGIT-A TRIAL

J.S. Vaidya[1] *, M. Bulsara[2], F. Wenz[3], S. Massarut[4], D. Joseph[5], J. Tobias[6], N.R. Williams[1], M. Baum[1], on behalf of the TARGIT Trialists Group. *[1]Division of Surgery and Interventional Science, University College London, London, United Kingdom, [2]Chair In Biostatistics, Institute of Health and Rehabilitation Research, University of Notre Dame, Fremantle, Australia, [3]Radiation Oncology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany, [4]CRO Centro di Riferimento Oncologia, Aviano, Italy, [5]Sir Charles Gairdner Hopsital, Perth, Australia, [6]Radiation Oncology, University College London Hospital, London, United Kingdom*

Goals: The Z-11 trial [1], found that even when axillary clearance is not performed after finding one or two positive sentinel nodes, it does not affect local control, despite 23% of patients in the axillary-clearance arm having positive nodes. However, every patient in this trial received whole breast radiotherapy and it has been suggested that inadvertent non-therapeutic irradiation of the lower axilla that occurs with tangential fields of conventional whole breast radiotherapy could be responsible for controlling the growth of the minimal residual axillary disease. Therefore, questions are being raised whether following the concept of sentinel node biopsy or not dissecting the axilla after 1–2 positive nodes is applicable to patients receiving partial breast radiation.

Methods: We compared the risk of axillary recurrence in patients with negative sentinel node biopsy or those with 1–2 positive nodes as per whether they received EBRT or TARGIT only within the updated TARGIT-A trial [2]. Please note that this is a comparison as per treatment received rather than as per randomised allocation.

Results: Overall there were 3375 patients who had breast conserving surgery. 1222 patients had a median follow up of 5 years, and all patients had a median follow up of 2 years 5 months. There are thus 9491 women-years of follow up. This trial patients had generally good prognosis but there were substantial number (>1200) patients ≤60 years, and more than 500 patients were node positive and/or grade 3. 91% of patients had sentinel node biopsy, of which 90% had <10 nodes removed if that was negative. 11 patients had axillary recurrences, one of whom had axillary clearance and other 10 had negative sentinel node biopsy. The risk of axillary recurrence was the similar whether the patients received EBRT [6/1762, 5-year risk 0.82% (95% CI 0.34–2.02)] or did not receive EBRT (5/1613, 5-year risk 0.68% (95% CI 0.28–1.6), HR 0.84 (0.26–2.74, $p = 0.8$). The results were similar if we only included patients with 1or 2 positive axillary nodes: EBRT given (1/255) vs. EBRT not given (0/127).

Conclusion: Omitting whole breast radiotherapy after a sentinel node biopsy in this good-prognosis population, is not associated with an increased axillary recurrence rate.

Reference(s)

[1] Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 2011; 305(6): 569–75.

[2] Vaidya JS, Wenz F, Bulsara M, et al. Targeted intraoperative radiotherapy for early breast cancer: TARGIT-A trial – updated analysis of local recurrence and first analysis of survival. San Antonio Breast Cancer Symposium, Dec 6, 2012. Cancer Res; 2012; 72(Suppl 24): 100s–101s.

Disclosure of Interest: I have received reimbursement for expenses to attend conferences, meetings and international steering committee meetings and honoraria from Carl Zeiss.

P235

FEWER NON-BREAST CANCER DEATHS IN TARGIT-A TRIAL: SYSTEMIC BENEFIT OF TARGIT OR LACK OF EBRT TOXICITY

J.S. Vaidya[1]*, M. Bulsara[2], F. Wenz[3], S. Massarut[4], D. Joseph[5], J. Tobias[6], N.R. Williams[1], M. Baum[1]. *[1]Division of Surgery and Interventional Science, University College London, London, United Kingdom, [2]Chair in Biostatistics, Institute of Health and Rehabilitation Research, University of Notre Dame, Fremantle, Australia, [3]Radiation Oncology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany, [4]CRO Centro di Riferimento Oncologia, Aviano, Italy, [5]Sir Charles Gairdner Hopsital, Perth, Australia, [6]University College London Hospital, London, United Kingdom*

Goals: TARGIT-A trial compared conventional fractionated external beam radiotherapy (EBRT), with the risk adapted approach using single dose targeted intraoperative radiotherapy (TARGIT); if TARGIT was given concurrently with lumpectomy and if high risk factors are found subsequently, EBRT had to be added (in 15–20% of cases). For the primary end point of ipsilateral breast recurrence, compared with EBRT, TARGIT achieved non-inferior local control in all cases and identical local control when given concurrently with lumpectomy in ER+PR+ cases. For the secondary endpoint of death, compared with EBRT, TARGIT had significantly fewer non-breast cancer deaths [1]. We investigated whether this difference could be explained by toxicity from EBRT.

Methods: 1. We compared cardiac deaths for left and right sided breast cancer. 2. We estimated cardiac deaths based on age, sex and follow up 3. We compared survival between the two randomised arms in the group that were randomised before lumpectomy – but limited to those who had received EBRT. Therefore, the control arm included patients who were allocated EBRT and received EBRT, and the experimental arm included patients who were allocated TARGIT and received EBRT in addition: as both groups received EBRT, any difference found was attributable to TARGIT.

Results: In the whole trial, there was a highly significant reduction in non-breast cancer mortality in the TARGIT arm (HR 0.47, p = 0.0086). 1. Cardiac deaths were 2 vs. 8 (TARGIT vs. EBRT), but were similar for each side: 1/775 vs. 4/795 for left; 1/776 vs. 4/746 right. 2. Amongst the 1730 patients randomised to receive EBRT, the 8 cardiac deaths were not higher than the 12 estimated based on age, sex and follow up period. 3. There were no deaths from non-breast cancer causes in the TARGIT+EBRT group compared with 24 in the EBRT group 0/218 vs. 24/892, log-rank p = 0.012.

Conclusion: Absence of a difference as per left or right side, a risk similar to age matched population, and the fact that patients who were allocated TARGIT+EBRT had significantly fewer deaths than those allocated EBRT, suggests that EBRT toxicity may not in itself have led to the non-breast cancer deaths and leads to the hypothesis that the local effect of TARGIT on the tumour bed by inhibiting the cancer-stimulating cytokines [2], may spill over to reduce systemic inflammatory response to trauma and have significant long-term systemic beneficial effects, that might be protective against cardiac and cancer mortality.

Reference(s)

[1] Vaidya JS, Wenz F, Bulsara M, et al. Targeted intraoperative radiotherapy for early breast cancer: TARGIT-A trial – updated analysis of local recurrence and first analysis of survival. Cancer Res; 2012; 72(Suppl 24): 100s-101s

[2] Belletti B, Vaidya JS, D'Andrea S, et al. Targeted intraoperative radiotherapy impairs the stimulation of breast cancer cell proliferation and invasion caused by surgical wounding. Clin Cancer Res. 2008; 14(5): 1325–1332.

Disclosure of Interest: I have received reimbursement of expenses for conferences, meetings and international steering committee meetings and honoraria from Carl Zeiss.

P236

PATIENTS' SUBJECTIVE EVALUATION IN PATIENTS WITH BREAST CANCER IRRADIATED WITH SHORT FRACTIONATION

M. Iwamoto*, A. Ikari, T. Tominaga, R. Terasawa, H. Fujioka, Y. Takahashi, K. Kimura, S. Tanaka, K. Uchiyama. *Breast Surgery, Osaka Medical College, Osaka, Japan*

Goals: The most commonly treatment plan of radiation threrapy for breast conserving surgery is 50 Gy in 25 fractions over 35 days (+ boost). Shorting of the radiation therapy treatment period is advantageous for patients unless the recurrence rate increases and radiation-related sequelae become exacerbated. In this study, we compared the frequency of "subjective" complications and their severity between 50 Gy in 25 fractions over 35 days and 44 Gy in 16 fractions over 22 days and analyzed the difference between the two groups.

Methods: Data from 350 patients with Stage I and Stage II breast cancer who underwent breast conserving surgery from1992 to 2003 were respectively analyzed. 196 patients and 154 patients received 50 Gy in 25 fractions over 35 days (Group C) and 44 Gy in 16 fractions over 22 days (Group S), respectively. Boost irradiation was performed in patients with a positive or closed margin, which was defined by pathologically proved tumor invasion within 5 mm from the cut end of the extirpated tissue. Early sequelae were evaluated at the end of radiation therapy (Point A) and 7–10 days after the radiation (Point B). Late sequelae were assessed at least 6 months after the end of the radiation (Point C). The presence or absence of the nine toxicities (hyperesthesia, intermittent pain, persistent pain, edema, pigmentation, teleangiectasia, sence of hardness, sense of thinness, sense of dryness) were evaluated.

Results: The most common toxicity at Point A was erythema in 153 (78.1%) and 115 (74.7%) patients [Group C/Group S] followed by heat sensation in 74 (37.8%) and 69 (44.8%) patients, sense of discomfort in 77 (39.3%) and 69 (40.9%) patients, and pain in 72 (36.7%) and 48 (31.2%) patients. There were no significant differences in these symptoms between Group C and Group S. The frequency of these symptoms hardly changed between Point A and Point B. At Point C, a sense of hardness more frequently appeared in Group S than in Group C with a significant difference (p = 0.01). Other commonly noted symptoms had no significant differences between the two groups. And, the ipsilateral breast tumor recurrence (IBTR) rate was 3.0% in Group C and 2.7% in Group S, with no significant difference between the groups.

Conclusion: Short fractionation results in acceptable patients "subjective" sequelae comparable to the sequelae comparable to the sequelae experienced following conventional fractionation. The time-sparing benefit of the short fractionation should thus be more widely recognized.

Disclosure of Interest: No significant relationships.

P237

INTERNAL MAMMARY LYMPH NODES IRRADIATION IN PATIENTS WITH BREAST CANCER

I. Abdel Halim*, W. El Sadda. *Clinical Oncology & Nuclear Medicine, Mansoura University, Mansoura, Egypt*

Goals: The purpose of the study is to evaluate the contribution of internal mammary nodal radiation to the benefit of postoperative radiotherapy in breast cancer patients as well as the impact on the overall survival (OS), the locoregional relapse free survival (LRRFS) and distant metastasis free survival (DMFS).

Methods: Between January 1999 and December 2004; breast cancer patients who were treated by either wide local excision or mastectomy followed by radiation therapy to the intact breast or chest wall and regional nodes were divided into 2 groups; gp A including patients treated without targeting of internal mammary chain (IMC) and gp B including patients treated with separate field targeting the IMC. The two groups (75 patients in each group) were

compared with respect to age, menopausal status, type of surgery, staging, pathology, number of axillary nodes involved, tumor grade, location of the tumor, ER/PR status and use of adjuvant systemic therapy. The data were obtained and reviewed retrospectively from the medical records.

Results: Baseline patients' characteristics were balanced between both groups with exception of T-stage; T3&T4 tumors were more likely to be encountered in gp B (72%) compared with 40% in gp A (P = 0.013). There were no significant difference between both groups at 5 years with respect to the OS (52% for gp A vs. 58.7% for gp B, P = 0.352) the locoregional relapse free survival (49.3% for gp A vs. 52% for gp B, P = 0.354) and distant metastasis free survival (46.6% for gp A vs. 44% for gp B, P = 0.837). The benefit of IMC irradiation was limited to patients with 4 or more positive axillary lymph nodes (N2–N3) as evidenced by better locoregoinal relapse free survival LRRFS (40% for no IMC vs. 58.6% for IMC. P = 0.048). Overall survival (OS) was better in N2–N3 patients who received a separate IMC field but did not reach the statistical significance (40% for no IMC vs. 57.3% for IMC P = 0.049).

Conclusion: Postoperative irradiation of IMC with separate field has no benefit with respect to survival parameters in breast cancer patients. It may be considered for patients with N2–N3 stage for better locoregional control.

Disclosure of Interest: No significant relationships.

Neoadjuvant (pre-operative) therapy

P240
A RETROSPECTIVE ANALYSIS OF PLATINUM-BASED NEOADJUVANT CHEMOTHERAPY FOR LATNBC

F. Fei *, Y. Du, G. Di, J. Lu, J. Wu, Z. Shao. *Breast Surgery, Shanghai Cancer Center Fudan University, Shanghai, China*

Goals: Purpose: We retrospectively analyzed platinum-based neoadjuvant chemotherapy for LATNBC to compare survival outcomes between patients with PCR and with non-PCR. Furthermore, the disease free survival of LATNBC patients with PCR continuously receiving primary regimen as adjuvant setting had comparative advantage concerning that of "PCR" patients switching to other regimens as adjuvant setting as well as those without any chemotherapy after surgery.

Methods: Patients and Methods: 124 women with stage II or III TNBCs experienced platinum-based regimens as neoadjuvant chemotherapy from Nov 1, 2007 to Dec 31, 2011. All patients were divided into the two groups, who were with and without PCR in the pathological reports after surgery. According to the adjuvant settings for LATNBC patients with PCR, the three arms were determined as continuous primary regimen (the same as neoadjuvant) arm, no more chemotherapy arm and switching arm. Disease free survival was computed using the Kaplan–Meier product limit method.

Results: Result: We presented a retrospective chart review of 124 LATNBC patients who underwent platinum-based neoadjuvant chemotherapy in our hospital. Fifty (40.32%) of those patients receiving neoadjuvant chemotherapy had PCR when they underwent surgery. After controlling for covariates associated with survival, patients undergoing neoadjuvant chemotherapy with residual tumor had significantly worse survival than patients with PCR (HR = 0.37, P < 0.05). Of 50 patients with PCR confirmed by surgery, the disease free survival of 24 cases switching to other regimens in the adjuvant setting was significantly better than that of 24 cases continuously receving primary regimens in the adjuvant setting (HR = 0.51, P = 0.025) and that of 2 cases with no more chemotherapy (HR = 0.58, P = 0.017).

Conclusion: Conclusion: Patients with PCR had statistically significantly better clinical survival than those with non-PCR after platinum-based neoadjuvant settings. So far, if LATNBC patients with PCR after platinum-based neoadjuvant chemotherapy, they might have better disease free survival if they receive switching regimens than to receive primary regimens and to continue with no additional chemotherapy after surgery. A randomized prospective study needs to be carried out to strengthen the results because of statistical bias.

Disclosure of Interest: No significant relationships.

P241
ANALYSIS OF COMPARATIVE EFFICACY OF NEOADJUVANT CHEMOTHERAPY REGIMENS IN BREAST CANCER

A. Aggarwal[1] *, N. Kouzminova[2], P. Rathi[2]. [1]*Medical Oncology, Santa Clara Valley Medical Center, California, United States of America,* [2]*Hematology/Oncology, Santa Clara Valley Medical center, California, United States of America*

Goals: Neoadjuvant chemo therapy is used to reduce the size and improve the respectability of tumor in locally advanced breast cancer. Various types of anthracyclin and taxane containing chemotherapies have been used. In this study we analyzed efficacy of commonly used neodajuvant chemotherapy regimens containing anthracyclin and taxane.

Methods: During 2005 and 2010, 47 patients with Stage through IV breast cancer were treated with neoadjuvant chemotherapy and underwent definitive surgery at SCVMC. 4 patients were excluded because they did not get any taxane as a part of chemotherapy. 9 patients received dose dense AC followed by weekly Paclitaxel (AC-T), 22 patients received FEC tri-weekly (every 3 weeks) followed by Docetaxel (FEC-D) tri-weekly, 3 patients received FEC followed by weekly Paclitaxel (FEC-T), and 4 patients received dose dense AC followed by Docetaxel (AC-D). 17/43 (39.5%) patients were her2neu positive and all of them received Trastuzumab as part of neoadjuvant chemotherapy.

Results: Pathological response was assessed after the definitive surgery. 5/43 (11.6%) patients did not respond (NR), 27/43 (62.8%) patients had partial response (PR) and 15/43 (34.9%) patients had complete or near complete response (CR). There was no significant difference in pathological response between different regimens (p-value = 0.64). When results were analyzed between chemotherapies containing AC or FEC, no difference was observed in the pathological response rate (p-value = 0.53). Similarly no difference was observed in pathological response rate when analyzed for paclitaxel vs. Docetaxel containing regimens (p-value = 0.60). Among stage III patients, 22 out of 31 patients received regimens containing Docetaxel rather than paclitaxel, but there was no difference in pathological response rate (p = 0.56) or tumor recurrence rate (0.90) Her2neu positive patients had higher rate of complete response than those who were her2neu negative as long as trastuzumab was used as part of neoadjuvant chemotherapy (50% vs. 25.9%; p = 0.026). There was no difference in response rate or tumor recurrence rate in her2neu positive patients between AC-T vs. FEC-D (p = 0.57), AC vs FEC (P-value = 0.40) or between P and D (p = 0.44). Fewer recurrences were seen in patients who achieved CR but the difference was not statistically significant (1/2 in NR, 6/25 in PR and 2/15 in CR, p = 0.4456). There was no difference in the tumor recurrence rate between regimens FEC/D vs. AC/T (p-value = 0.9454), Paclitaxel vs. Docetaxel (p-value = 0.7307), or FEC vs. AC (p-value = 0.77). No correlation with age (<45 vs. >45) was observed between any of the above comparisons.

Conclusion: Dose dense AC/T is comparable to FEC/D in efficacy as Neoadjuvant chemotherapy in breast cancer patient. Her2neu positive breast cancer patients have higher pathological CR rate compared with her2neu negative patients as long as trastuzumab is used as a part of neoadjuvant chemotherapy.

Disclosure of Interest: No significant relationships.

P242

PREDICTIVE BIOMARKERS OF NEOADJUVANT CHEMOTHERAPY EFFECTS AND ADVERSE EVENTS

K. Takagi*, K. Nakao, M. Oikawa, T. Miyazaki, A. Matsumoto, R. Otsubo, M. Matsumoto, H. Yano, T. Nagayasu. *Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Science, Nagasaki, Japan*

Goals: Reactive oxygen species (ROS) function as key metabolites that can impair biological processes, resulting in various pathological conditions. The aims of this study were to assess the changes over time in oxidative stress and antioxidant potential in breast cancer patients who underwent chemotherapy, and to evaluate the correlations of oxidative stress and antioxidant potential with adverse events or effectiveness of chemotherapy and various clinicopathologic characters.

Methods: We measured the levels of blood hydroperoxides, a type of ROS, as an index of oxidative injury to cellular components, as well as the plasma ferric-reducing ability as an index of total antioxidant potential, among breast cancer patients with adjuvant chemotherapy. Hydroperoxides were spectrophotometrically measured by the levels of diacron reactive oxygen metabolites (d-ROMs). The antioxidant potential was spectrophotometrically determined by the biological antioxidant potential (BAP), which represents the levels of endogenous antioxidant enzymes. These tests were performed using a FREE analyzer (Wismerll Co. Ltd., Tokyo, Japan). Serum samples were collected from breast cancer patients with adjuvant chemotherapy (5FU, epirubicin, cyclophosphamide (FEC) followed by docetaxel (DOC) or FEC only) in Nagasaki University Hospital and Japanese Red Cross Nagasaki Atomic Bomb Hospital. Adverse events of chemotherapy were evaluated using the Common Terminology Criteria for Adverse Events v4.0, and effectiveness of chemotherapy was evaluated using the response evaluation criteria in solid tumors. The study protocol was approved by each Hospital Ethics Committee.

Results: The d-ROM levels in patients with chemotherapy were significantly higher than those in patients before chemotherapy (442.0±62.81 vs. 359.5±85.2 U.Carr, p = 0.0073; U.Carr: 1 U.Carr corresponds to 0.8 mg/L H_2O_2). The BAP decreased after DOC administration (2175.7±226.3 vs. 2027.8±200.5 μmol/L, p = 0.0186). Regarding effectiveness of chemotherapy, the d-ROM levels in complete response patients were significantly lower than those in partial response patients (382.5±63.1 vs. 471.3±112.5 U.Carr, p = 0.0013). The d-ROM levels in patients who developed anemia of more than Grade 2 were significantly higher than those in patients with anemia of less than Grade 1 (413.6±83.5 vs. 464.3±112.6 U.Carr, p = 0.0213). The BAP showed no significant correlations among chemotherapy effects and adverse events.

Conclusion: Chemotherapy generates large amounts of ROS. The BAP decreases after a prolonged course of chemotherapy. The marked effects of chemotherapy may reduce tumor-derived ROS. Anemia, one of the adverse events of chemotherapy, was significantly correlated with the increase in d-ROMs. d-ROMs may potientially be one of the predicting factor of chemotherapy effects and adverse effects.

Disclosure of Interest: No significant relationships.

P243

NODAL COUNTS AND RATIO FOLLOWING PRIMARY CHEMOTHERAPY: AN ALTERNATIVE TO TRADITIONAL PN STAGING

S. Chen*, Y. Liu, L. Huang, K. Yu, J. Wu, Z. Shao. *Breast Surgery, Shanghai Cancer Institution/Centor, Shanghai, China*

Goals: Neoadjuvant chemotherapy (NCT) for breast cancer might change the number of involved and detected nodes in axillary lymph node dissections (ALND). In this study, we analyzed whether the number of dissected nodes and the lymph node ratio (LNR, defined as the proportion of involved nodes in dissected nodes) would have a better prognostic value than traditional pN staging.

Methods: In total, 569 patients with stage II-III breast cancer were included in this retrospective study. All patients underwent a median of 3 cycles of NCT followed by mastectomy and ALND at the Shanghai Cancer Center. Clinical and pathological variables were investigated using univariate and multivariate survival analyses. The prognostic value of the LNR was calculated categorically in increments of 20%.

Results: The median follow-up time was 48 months. In post-NCT node-negative patients, the number of dissected nodes was an independent prognostic indicator on multivariate analysis (P = 0.002). Those with 4–9 dissected nodes experienced a significantly lower relapse-free survival (RFS) compared with those with 10 or more dissected nodes (HR = 0.19, 95% CI 0.07 to 0.46 for 10–19 nodes; HR = 0.41, 95% CI 0.42 to 1.41 for 20+ nodes; 4–9 nodes as the reference). In post-NCT node-positive patients, a lower LNR was correlated with a better RFS on multivariate analysis, and pN staging failed to show independent prognostic significance when the LNR was included in the Cox regression model (HR = 4.20, for LNR 81–100%, HR = 2.97 for LNR 61–80%; HR = 2.24 for LNR 41–60%; HR = 1.68 for LNR 21–40%; LNR 0–20% as the reference. P < 0.001). In addition, there were significant differences in the estimated 5-year RFS for pN1 (P = 0.043) and pN3 patients (P = 0.030) among the different LNR subgroups.

Conclusion: Our study has provided new evidence that the number of dissected nodes (in pN− patients) and the LNR (in pN+ patients) might be a complementary or alternative method to traditional pN staging when evaluating disease after primary treatment and tailoring further therapeutic strategies. Further prospective studies are warranted on a larger scale to establish this as a reliable staging technique.

Disclosure of Interest: No significant relationships.

P244

NABRAX: NAB-PACLITAXEL AS NEOADJUVANT THERAPY OF BREAST CANCER: INTERIM SAFETY OF GEICAM 2011–02

S. Antolín[1]*, J.I. Chacón[2], A. Antón[3], M.Á. Seguí[4], P. Sánchez-Rovira[5], A. Plazaola[6], E. Espinosa[7], Á. Guerrero[8], E. Carrasco[9], M. Martín[10]. *[1]Oncology Department, Complejo Hospitalario de la Coruña, A Coruña, Spain, [2]Hospital Universitario Virgen de la Salud, Toledo, Spain, [3]Hospital Universitario Miguel Servet, Zaragoza, Spain, [4]Corporación Sanitaria Parc Taulí, Barcelona, Spain, [5]Complejo Hospitalario de Jaén, Jaén, Spain, [6]Onkologikoa, San Sebastián, Spain, [7]Hospital Universitario La Paz, Madrid, Spain, [8]Instituto Valenciano de Oncología, Valencia, Spain, [9]GEICAM headquarters, Madrid, Spain, [10]Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain*

Goals: Nab-paclitaxel is an innovative chemotherapy that consists of nanometer-range particles of human serum albumin bound paclitaxel. It exploits the role of albumin as the natural carrier of hydrophobic molecules in human to increase paclitaxel delivery to tumor cells. Weekly nab-paclitaxel showed a superior efficacy compared to every 3-weeks docetaxel in a randomized phase II study in metastatic breast cancer (BC) (Gradishar JCO 2009). This trial has been designed to evaluate the activity and safety of weekly nab-paclitaxel as neoadjuvant treatment of early stage BC patients with positive estrogen receptors and negative HER2.

Methods: Seventy-eight patients will be included and treated with nab-paclitaxel weekly at a dose of 150 mg/m^2 on days 1, 8 and 15 every 4 weeks for 4 cycles. Following chemotherapy, they will undergo surgery and adjuvant treatment (with radiation, chemo and endocrine therapy) under the investigator criteria. The primary objective is to determine the residual cancer burden III measured by the Symmans criteria. Secondary objectives include pathological

complete response, overall response, invasive disease free survival, safety and biomarkers.

Results: Sixty-three patients have been recruited to date; here we report safety data from 48 patients. Median age was 52 years (28–70), 45% were postmenopausal and 94% had ECOG PS 0; 54% of patients were T2, and 29% were T3; 44% were N0, 29% N1 and 4% N2; most patients were stage II (25% IIa and 40% IIb). A total of 118 cycles have been administered to date; 13 patients completed 4 cycles as planned, one patient discontinued treatment early due to grade 3 peripheral neuropathy after the third cycle, the remaining patients are still under treatment. Four dose administrations of nab-paclitaxel were omitted, fifteen were reduced (13 to 125 and 2 to 100 mg) and two cycles were delayed (7 and 8 days), for a relative dose intensity of 86%. The most frequent reasons for dose modifications were neutropenia (9 doses) and neurotoxicity (5 doses). The main grade 2/3 toxicities per cycle were alopecia (41%), neuropathy (6.8%/2.5%), fatigue (7.6%/0.8%), neutropenia (6.8%/4.2%) and arthralgia (3.4/0%) in 20, 8, 8, 11 and 3 patients respectively.

Conclusion: Nab-paclitaxel was well tolerated as neoadjuvant therapy in this patient population. Updated safety data will be presented at the meeting.

Disclosure of Interest: Dr. A. Anton receive research and travel support.

P245

PATHOLOGICAL COMPLETE RESPONSE RATE BY SUB-TYPES AFTER NEOADJUVANT TREATMENT FOR BREAST CANCER

A. Bourbonnais*, C. Prady, S. Fox, P. Desjardins, R. Simon, C. Matte, M. Billy, J. Latreille. *Heamato-Oncology, Charles-Lemoyne Hospital, University Sherbrooke, Greenfield Park, Canada*

Goals: To determine the overall pathological complete response (pCR) rate and the pCR rate according to commonly described breast cancer sub-types in our population.

Methods: This retrospective study, from a single institution, analyzes patients with breast cancer treated with neoadjuvant chemotherapy or hormonal therapy between 2006 and 2011. pCR rate, defined as ypT0N0 excluding patients with DCIS, was determined according to sub-types: luminal A and B/her2 negative, luminal B/her2 positive, triple negative, and her2 positive disease.

Results: A total of 131 women, with a median age of 56 years old, were classified as follow: luminal A and B/her2 negative 68 (51.9%), luminal B/her2 positive 18 (13.7%), triple negative 23 (17.6%), her2 positive disease 22 (16.8%). Breast cancer histological types were: invasive ductal carcinoma 85%, invasive lobular carcinoma 11% and other pathologies 4%. Clinical stage I represented 6% and stage II and III 94% of the population. Neoadjuvant treatment consisted of chemotherapy for 88% and hormonal therapy for 12% of patients. Among the 131 patients, overall pCR rate is 14% (18). pCR rate by sub-types: luminal A and B/her2 negative 6% (4/68), luminal B/her2 positive 17% (3/18), triple negative 32% (7/22) and her2 positive disease 17% (4/22). All 18 patients with pCR received chemotherapy as neoadjuvant treatment. One patient had clinical stage I (luminal B/her2 negative) and the 17 (94%) remaining were clinical stage II and III. Surgery for these patients was breast conservative (13) or modified radical mastectomy (5). At a median follow-up time of 34.5 months, 17 (94%) are still in remission and one death occurred caused by progressive brain metastases (triple negative).

Conclusion: Our results for pCR are concordant with the literature for luminal A and B/her2 negative, luminal B/her2 positive and triple negative disease. However, it is difficult to explain the low rate achieved in her2 positive disease. Duration of response among pCR patients is also in line with published data. The low pCR rate of luminal A and B/her2 negative disease questions the relevance of neoadjuvant treatment if initial breast conservative surgery is feasible.

Disclosure of Interest: No significant relationships.

P246

A MULTI-CENTER, SINGLE-ARM STUDY OF NEOADJUVANT CHEMOTHERAPY COMBINED WITH LETROZOLE

E. Sakata[1]*, C. Kanbayashi[2], N. Sato[2], K. Kaneko[2], Y. Koyama[1], T. Sato[3], I. Muto[3], K. Honma[4], K. Akazawa[5], M. Sano[6]. *[1]Departments of Surgery, Niigata University Medical and Dental Hospital, Niigata, Japan, [2]Departments of Surgery, Niigata Cancer Center Hospital, Niigata, Japan, [3]Departments of Surgery, Niigata Prefectural Central Hospital, Niigata, Japan, [4]Departments of Pathology, Niigata Cancer Center Hospital, Niigata, Japan, [5]Department of Medical Informatics, Niigata University Medical and Dental Hospital, Niigata, Japan, [6]Niigata Breast Exam Center, Niigata, Japan*

Goals: To investigate if chemo-endocrine therapy improves pathological CR (pCR) for patients with endocrine-responsive breast cancer, we designed a single-arm study of neoadjuvant chemotherapy with letrozole (LET) to assess the pCR rate for postmenopausal women with stage II-IIIA, ER and/or PR positive breast cancer.

Methods: Patients were treated with a neoadjuvant regimen of doxorubicin 60mg/m^2 or epirubicin 90mg/m^2 plus cyclophosphamide 600mg/m^2 Q3 (AC/EC) $\times$ 4 cycles followed by paclitaxel (Pac) 80 mg/m^2 $\times$ 12 weeks and concurrently letrozole, 2.5mg/day (P.O.) prior to surgical treatment of their breast cancer. Patients were followed for tumor assessment (palpation and ultrasound) at 3 week intervals for first 12 weeks and 6 week intervals for last 12 weeks. CT/MRI scans were carried out prior to therapy and 24 weeks after initiation of therapy. Pathological response was evaluated by each local laboratory in the participating centers. As an early-stopping rule, the protocol specified that the study should be stopped if no pCR was observed in the first 20 patients.

Results: As of March 2011, 20 patients in 4 centers had completed protocol treatment. The median age was 59 years old (range: 50–68). There was no pCR in the patients. According to MRI or CT scan, CR was observed in 1 (5.5%), PR in 11 (61.1%), SD in 5 (27.8%) and PD in 1 (5.5%). The overall response rate was 66.6%. Breast conserving surgery rate was 79%. Grade 3/4 (CTCAE v3.0) toxicities were white blood cell decreased 55/21% (AC or EC/Pac), neutrophil count decreased 75/21% (AC or EC/Pac) and febrile neutropenia 5/0% (AC or EC/Pac).

Conclusion: Although AC/EC followed by paclitaxel combined with letrozole was safe and tolerable in endocrine-responsive postmenopausal breast cancer patients, it didn't improve the pCR rate in this setting.

Disclosure of Interest: No significant relationships.

P247

PATHOLOGICAL COMPLETE RESPONSE PREDICTS FOR SURVIVAL IN ALL SUBTYPES (EORTC 10994/BIG 1-00)

H. Bonnefoi[1]*, S. Litière[2], M. Piccart[3], P. Fumoleau[4], E. Brain[5], T. Petit[6], J. Jassem[7], T. Cufer[8], J. Bergh[9], D. Cameron[10]. *[1]Medical Oncology, Institut Bergonié Cancer Center, Bordeaux, France, [2]European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium, [3]Medicine, Institut Jules Bordet, Brussels, Belgium, [4]Centre G-F Leclerc, Dijon, France, [5]Curie St-Cloud, Paris, France, [6]Centre Paul Strauss, Strasbourg, France, [7]Medical University, Gdansk, Poland, [8]University Clinic Golnik, Ljubljana, Slovenia, [9]Karolinska Institutet, Stockholm, Sweden, [10]Edinburgh University, Edinburgh, United Kingdom*

Goals: pCR following chemotherapy is a proven surrogate for survival, although its predictive value may be restricted to specific subtypes. In this analysis we assessed: (1) the effect of pCR on event-free survival (EFS), distant metastasis-free survival (DMFS) and overall survival (OS) by intrinsic subtype (using the St.Gallen 2011 shorthand classifier); (2) the prognostic value of TP53 (functional yeast assay) and chemotherapy type on the survival endpoints within intrinsic subtypes (interaction tests).

Methods: This is a planned substudy of a previously reported phase 3 study. Patients received either 6 cycles of anthracycline-based chemotherapy or 3 cycles of docetaxel à 3 cycles of eprirubicin/docetaxel (T-ET). This analysis was limited to patients with known HER2, ER, PR status and grade (a substitute of Ki67). pCR was defined as no evidence of residual cancer (with or without residual DCIS) in the primary tumor and lymph nodes (ypT0/is, ypN0). No patients received neoadjuvant trastuzumab. A landmark method was used starting from date of surgery with hazard ratios calculated using multivariate Cox models (alpha ≤0.01). Interactions were studied in a Cox model between pCR, TP53, treatment arm and intrinsic subtypes on EFS (alpha = 0.1 for inclusion in multivariate analysis).
Results: pCR occurred in 222/1212 (18%) evaluable patients: 37/496 (7.5%) luminal A, 22/147 (15%) luminal B/HER2-negative, 51/230 (22%) luminal B/HER2-positive, 43/118 (36%) HER2-positive/non luminal, 69/221 (31%) triple negative. pCR and treatment arm were independent predictors of EFS (HR = 0.40, $p < 0.001$ in favour of pCR, and HR = 0.73, $p = 0.004$ in favor of T-ET). The prognostic effect of pCR on EFS did not differ between the subtypes (interaction test $p = 0.95$), and was an independent predictor for DMFS (HR = 0.35, $p < 0.001$) and OS (HR = 0.32, $p < 0.001$). Only the interaction between TP53, intrinsic subtypes and EFS approached statistical significance ($p = 0.1$), suggesting that the effect of TP53 may differ according to subtypes. No interaction was found for DMFS and OS. TP53 was not an independent predictor for pCR ($p = 0.27$), while intrinsic subtype was a strong predictor ($p < 0.001$).
Conclusion: This analysis confirms that pCR is a strong favorable predictor of clinical outcome in all intrinsic subtypes. This effect is most apparent in triple negative and luminal B/HER2-negative subtypes.
Disclosure of Interest: No significant relationships.

P248
THE ASSOCIATION OF CHANGES IN BIOMARKERS WITH PATHOLOGIC RESPONSE TO NEO-ADJUVANT CHEMOTHERAPY

T. Kim[1]*, S. Jung[2], J. Choi[3]. [1]*Surgery, Inje University, Busan Paik Hospital, Busan, South Korea,* [2]*Pathology, Inje University, Busan Paik Hospital, Busan, South Korea,* [3]*Seoul National University College of Medicine, Seoul, South Korea*

Goals: Neo-adjuvant chemotherapy (NAC) induced variations in HR status in 23% of patients. A positive switch in HR status after NCT could be an indicator of better prognosis for patient outcome (Tacca O et al. Oncologist 2007; 12: 636). Residual cancer burden (RCB) determined from routine pathologic materials was a significant predictor of Distant relapse-free survival (Symmans WF et al. JCO 2007; 25: 4414). This study investigated the relation between RCB and the changes of biomarkers after NAC.
Methods: We applied NAC in 58 patients of breast cancer between May 2008 and Oct 2012. The patients with nodal involvement received combined anthracycline and taxane chemotherapy, meanwhile patients with nodal negative received anthracycline-based therapy. We evaluated pathologic response to NAC by using RCB system. We were able to obtain 54 paired specimens before and after chemotherapy for Immunohistochemical staining (IHC) of biomarkers such estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67. We analyzed the association of the changes of biomarkers with RCB.
Results: RCB 0 (pathologic complete response) occurred in 5 patients (8.6%), RCB I [minimal residual disease (RD)] did in 3 patients (5.2%), RCB II (moderate RD) did in 37 (63.8%), and RCB III (extensive RD) did in 13 patients (22.4%). The changes of molecular biomarkers have been observed after NAC in breast cancer: ER decreased in 4 (8.2%), PR decreased in 14 (28.66%), HER2 increased in 8 (16.3%) and decreased in 5 (10.2%), and Ki67 decreased in 29 (59.2%). In 3 cases of RCB1 ER was not changed, PR was not changed, HER2 was decreased in 1 (33.3%), Ki67 was decreased in 3 (100%). In 35 cases of RCB II ER was increased in 1 (2.9%) and decreased in 3 (8.6%), PR was increased in 1 (2.9%) and decreased in 11 (31.4%), HER2 was increased in 6 (17.1%) and decreased in 3 (8.6%), and Ki67 was increased in 1 (2.9%) and decreased in 21 (60%). In 11 cases of RCB III ER was decreased in 1 (9.1%), PR was decreased in 3 (27.3%), HER2 was increased in 2 (18.2%) and decreased in 1 (9.1%), and Ki67 was decreased in 5 (45.5%). The changes of ER, PR HER2 and Ki67 did not affected to RCB. Ki67 did not predictive factor for chemotherapy. Intrinsic subtype by IHC would be changed by chemotherapy.
Conclusion: The changes of molecular biomarkers have been observed after neoadjuvant chemotherapy in breast cancer. The intrinsic subtypes by IHC also could be changed between before and after neoadjuvant chemotherapy. These changes of biomarkers would be due to molecular down-regulation and development of compensatory pathway. We need to examine again biomarkers in tissue obtained by surgery in order to establish a therapeutic strategy after mastectomy in neoadjuvant setting of breast cancer.
Disclosure of Interest: No significant relationships.

P249
SAFETY OF 150 mg/m² NAB-PACLITAXEL WEEKLY EITHER AS WEEKLY OR AS 300 mg/m² BIWEEKLY REGIMEN

S. Loibl[1]*, M. Untch[2], C. Jackisch[3], H. Wiebringhaus[4], H. Forstbauer[5], G. Wachsmann[6], Z. Maczynska[7], V. Nekljudova[7], G. von Minckwitz[8], V. Möbus[9]. [1]*Medicine and Research, German Breast Group, Neu-Isenburg, Germany,* [2]*Frauenklink, Helios Kliniken, Berlin, Germany,* [3]*Klinikum Offenbach, Offenbach, Germany,* [4]*St. Barbara-Klinik Heessen, Hamm, Germany,* [5]*GOSPL Gesellschaft für onkologische Studien, Troisdorf, Germany,* [6]*Klinikum Sindelfingen-Böblingen / Kliniken Böblingen, Böblingen, Germany,* [7]*German Breast Group, Neu-Isenburg, Germany,* [8]*GBG Forschungs GmbH, Neu-Isenburg, Germany,* [9]*Klinikum Frankfurt Höchst GmbH, Höchst, Germany*

Goals: Nab-paclitaxel is an albumin bound non-particle formulated paclitaxel. Several studies have shown that the weekly application might be more efficacious than the three weekly dosage of 260 mg/m².
Methods: Within the neoadjuvant GeparSepto trial (NCT01583426) and the dose-intensified adjuvant GAIN-2 trial in primary breast cancer (NCT01690702), the nab-paclitaxel dose of 150 mg/m²/week will be further evaluated. In the GeparSepto trial weekly 150 mg/m² are compared to weekly 80 mg/m² paclitaxel both given for 12 weeks, followed by epirubicin (90 mg/m²) / cyclophosphamide (600 mg/m²) (EC) in both arms prior to surgery. All patients with HER2+ disease will receive trastuzumab and pertuzumab. Primary endpoint is pathological complete response. In the adjuvant GAIN-2 trial for high risk pN0–1 or pN2 primary breast cancer 3 cycles 150 mg/m² bi-weekly epirubicin followed by 3 cycles bi-weekly 300 mg/m² nab-paclitaxel followed by 3 cycles 2 g/m² cyclophosphamide are compared to a tailored dose-dense regimen consisting of EC followed by docetaxel. Primary endpoint is invasive disease free survival. In the GeparSepto trial the safety of the first 30 patients in the nab-paclitaxel arm will be analysed. In the GAIN-2 trial, the final dose of nab-paclitaxel will be evaluated during an integrated run-in phase based on the rate of febrile neutropenia and grade 3–4 sensory neuropathy observed in the first 15 patients. The final dose will be either deescalated to bi-weekly 260 mg/m², remain 300 mg/m², or escalated to 330mg/m².
Results: The baseline characteristics are well balanced. In the GeparSepto trial the median age is 49.5 years (29–73). 28% cT1, 88% ductal carcinoma, 57%cN0, 57% G3, 100% HER2-, 62% ER/PgR positive, 55% Ki67 >20%, 80% SPARC negative In the GAIN-2 trial the median age is 48 years (37–62). High risk categories are distributed as follows HR+/HER2-; Ki67 <20% with LN ≥4: 20%; HR+/HER2–

Ki67 >20%: 13%; HR+/HER2+10%; HR-/HER2+ 17%; TNBC 40%. pN0–1: 47%; pN2: 40%; pN3: 13%.
In the GeparSepto trial overall 12 serious adverse events have been reported in 135 patients so far included in the trial, 9 in the nab-paclitaxel arm and 3 in the paclitaxel arm. In the GAIN-2 trial overall 2 SAEs have been reported during epirubicin in 53 patients so far recruited.
Conclusion: So far, the regimens seem feasible. The final results of these safety interim analyses will be presented at the meeting.
Disclosure of Interest: No significant relationships.

P250
CARDIAC SAFETY OF PERTUZUMAB- AND TRASTUZUMAB-BASED THERAPY: NEOSPHERE AND TRYPHAENA JOINT ANALYSIS

L. Gianni[1]*, J. De La Haba-Rodriguez[2], C. Tausch[3], B. Bermejo[4], V. Mcnally[5], J. Ratnayake[6], E. Clark[5], G. Ross[5], A. Schneeweiss[7]. *[1]Department of Medical Oncology, Hospital San Raffaele, Milan, Italy, [2]Hospital Universitario Reina Sofia, Cordoba, Spain, [3]Breast-Center, Zurich, Switzerland, [4]Servicio De Hematologia Y Oncologia Medica, Hospital Clinico de Valencia, Valencia, Spain, [5]Roche Products Limited, Welwyn, United Kingdom, [6]Roche Diagnostics Limited, Penzberg, Germany, [7]National Center for Tumor Diseases, Heidelberg, Germany*

Goals: Trastuzumab (H) and chemotherapy (Ct) compared with Ct alone is associated with a considerable increase in pathological complete response (pCR) in HER2-positive early breast cancer (EBC). Pertuzumab (P) when combined with H-based therapy has been shown to improve activity without any substantial increase in adverse events, particularly cardiac. We report updated data after longer follow-up from two neoadjuvant Phase II studies, NeoSphere and TRYPHAENA, with H, P and Ct.
Methods: Patients (pts) had HER2-positive EBC. Left ventricular ejection fraction of ≥55% at baseline was required. Neoadjuvant treatment combining H and P with anthracycline-based or anthracycline-free Ct regimens was given for 4 (NeoSphere) or 6 (TRYPHAENA) cycles, q3w. In NeoSphere, H+P was given without Ct in one arm; in another arm, P was given with docetaxel (T) without H. All arms in TRYPHAENA contained H+P plus a Ct regimen. Primary endpoints were pCR in the breast (ypT0/is; NeoSphere) and cardiac safety (TRYPHAENA). After surgery, adjuvant H was given to complete 1 year of treatment. Pts in NeoSphere also received adjuvant Ct per protocol.
Results: 417 (NeoSphere) and 225 (TRYPHAENA) pts were enrolled. In NeoSphere, 356/417 pts (85%) and in TRYPHAENA, 186/225 (83%) pts completed adjuvant treatment. No patient was still receiving adjuvant treatment at the time of this analysis. Median time on study was 37 months for NeoSphere versus 22 months for TRYPHAENA and balanced across arms in NeoSphere and TRYPHAENA, respectively. Pts who experienced symptomatic left ventricular systolic dysfunction (sLVSD) (grade ≥3) are presented in the table. During the neoadjuvant and adjuvant periods for both studies combined, 4 additional pts experienced serious adverse events of LVSD, which were considered asymptomatic. In NeoSphere, pCR was significantly improved with T+H+P (45.8%) versus T+H (29.0%); high pCR rates were observed in TRYPHAENA in all arms (57–66%).

	sLVSD in safety population, n/N (%)			
	FEC → T+H+P n = 75	H+P n = 108	T+H+P+carboplatin n = 76	Other H±P+Ct combinations n = 380
Neoadjuvant	2/75 (2.7)	1/108 (0.9)	–	–
Adjuvant	–	–	1/67 (1.5)	–
Follow-up	1/75 (1.3)	–	–	–

FEC, 5-fluorouracil, epirubicin, cyclophosphamide.

Conclusion: Results showed that the combination of P with H+T in HER2-positive EBC significantly improved the activity of H+T. The overall incidence of sLVSD was low, even with this longer follow-up period.
Disclosure of Interest: LG discloses a consultant/advisory role for Roche/Genentech, GlaxoSmithKline, Novartis, Pfizer, Boehringer Ingelheim, AstraZeneca, Celgene, BioScience and Tahio.

P251
STUDY OF PATIENTS WITH STAGE III BREAST CANCER WHO RECEIVED NEOADJUVANT CHEMOTHERAPY

N. Iwakuma*, U. Toh, R. Takahashi, M. Mishima, M. Takenaka, K. Koura, T. Fujii, K. Shirouzu. *Surgery, Kurume University School of Medicine, Kurume, Japan*

Goals: Despite the good responses to neoadjuvant chemotherapy (NAC) in patients with stage III breast cancer, most eventually relapse and have a poor prognosis. We investigated prognostic indicators in stage III breast cancer patients treated with NAC, using epirubicin and/or docetaxel.
Methods: A total of 22 women with stage III breast cancer underwent NAC between January 2005 and May 2011. The regimens of NAC composed of ED (epirubicin 60 mg/m^2, docetaxel 60 mg/m^2) in 10 cases, FEC (5-FU 500 mg/m^2, epirubicin 75–100 mg/m^2, cyclophosphamide 500 mg/m^2) in 10 cases, and EC (epirubicin 60 mg/m^2, cyclophosphamide 600 mg/m^2) in 2 cases. After 4 cycles of each regimen, further 4 cycles of D (docetaxel 70 mg/m^2) was followed in 9 cases. After achieving NAC and surgery, we assessed clinicopathological findings. Statistical analyses associated with disease-free survival (DFS) or overall survival (OS) was conducted.
Results: The median survival time was 66 months, and there were 12 distant metastases and 2 local recurrences. Multivariate analyses showed the number of metastatic axillary lymph nodes (ALN) was associated with DFS, while Ki-67 labeling index and the number of metastatic ALN were associated with OS.
Conclusion: Even if stage III breast cancer patients show good responses to NAC using epirubicin and/or docetaxel, most eventually relapse and have a poor prognosis. Ki-67 labeling index and the number of involved ALN are suggested as prognostic indicators in stage III breast cancer.
Disclosure of Interest: No significant relationships.

P252
FIRST SAFETY ANALYSIS OF HPC AND HPE AS NEOADJUVANT THERAPY IN BREAST CANCER PATIENTS WITH HER2+

L. Huang[1]*, S. Chen[1], B. Xu[2], T. Huang[3], H. Yang[4], H. Zheng[5], Y. Wang[6], E. Song[7], J. Zhang[8], Z. Shao[1]. *[1]Department of Breast Surgery, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China, [2]Department of Medical Oncology, Cancer Hospital & Institute, Chinese Academy of Medical Sciences, Beijing, China, [3]Department of Breast and Thyroid Surgery, Wuhan Union Hospital, Wuhan, China, [4]Department of Breast Surgery, Department of Breast Surgery, Zhejiang Cancer Hospital, Zhejiang, Zhejiang, China, [5]West China Hospital, Chengdu, China, [6]Department of Breast Surgery, Shandong Cancer Hospital, Zhejiang, Jinan, China, [7]Sun Yat-Sen Memorial Hospital, Guangzhou, China, [8]3rd Department of Breast Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China*

Goals: Neoadjuvant chemotherapy may provide an early indication of treatment effect and pathologic complete response (pCR) rate is a surrogate measure of disease-free and overall survival. Anthracyclines remain an important component of chemotherapy regimens for breast cancer (BC), adding a taxane conveys additional survival benefit. However the combine of anthracycline and trastuzumab is still controversy, because of potential increased risk of cardiac event. This trial was designed to compare the efficacy and

safety between epirubicin (E) and carboplatin (C) in combination with Paclitaxel (P) and trastuzumab (H).

Methods: 100 Patients with HER-2/neu immunohistochemistry (IHC) 3+ or fluorescent in situ hybridization (FISH)-amplified untreated breast cancer, baseline left ventricular ejection fraction (LVEF) of ≥55%, ECOG0/1, were enrolled from Sep 2011 to May 2012. Study medication was as follows: Trastuzumab (4 mg/kg loading dose followed by 2 mg/kg) and Pacitaxel (75 mg/m^2) weekly combine with Carbopatin (AUC 2) weekly for HPC group or Epirubicin (75 mg/m^2) every 3 weeks for HPE group. Patients were recommended to receive 4 or 6 cycles. The prime endpoint was pCR, the second endpoints included clinical response, safety and translational research.

Results: By May 14, 2012, 50 patients were randomly assigned to receive HPC regimen and 50 to receive HPE regimen from 13 medical centers. 48 belonged to TNM stage II, 51 belonged to TNM III. The median age was 48 years (range, 29 to 65 years). 38 patients completed at least 4 cycles neoadjuvant therapy. Common grade 3or 4 grade hematologic toxicities were neutropenia, 19 patients in HPC and 20 patients in HPE. 11 patients in HPC and 16 patients in HPE had 3 or 4 grade leucopenia. 5 patients in HPC and 1 patient in HPE had 3 or 4 grade transaminase elevation. Median LVEF at baseline was 66.0% (range, 56.5% to 83.0%), there was no difference in HPC and HPE group (67.0% vs. 65.0%). After 2 cycles in 62 of 100 patients, the median LVEF was 65% (range 55.6% to 76.1%), there was no difference about the LVEF in HPC group and HPE group (64.5% vs. 65.0%). 5 patients had left ventricular ejection fraction (LVEF) decreases over 10%, 2 (6.3%) patients in HPC group and 3 (10.0%) patients in HPE group. After more than 4 cycles in 38 of 100 patients, LVEF was 65% (range, 53.0% to 73.0%), 3 patients had LVEF decreases over 10.0% compared with baseline, all 3 (15.7%) patients in HPC, no difference was found between the two group (63.5% vs. 66.1%). No patient experienced LVEF less than 50.0% and congestive heart failure (CHF). There were no cardiac deaths.

Conclusion: Both HPC and HPE regimens as neoadjuvant chemotherapy are tolerable for the treatment of her2 overexpression breast cancer patients. HPE is feasible and is not likely to increase the incidence of acute cardiac events compared to HPC, while the HPE regimen has disadvantages with more grade III/IV hematologic toxicities.

Disclosure of Interest: No significant relationships.

P253

COMPARING IHC CHANGE ON RADIOTHERAPY AND ANTRACYCLYNE-BASED CHEMOTHERAPY USING P53 AS PREDICTOR

R. Yohana[1]*, D. Ahmad[2], H. Agustina[3]. [1]*Oncology, Head and Neck Surgery Departement, Padjadjaran University, Bandung, Indonesia,* [2]*Oncology, Head and Neck Surgery, Padjadjaran University, Bandung, Indonesia,* [3]*Padjadjaran University, Bandung, Indonesia*

Goals: To minimize local recurrent rate and improve the quality of life and also to verify the role of p53 expression and IHC change in local effect to determine LABC patients who received anthracycline based neoadjuvant chemotherapy or primary radiotherapy.

Methods: Two groups of 64 LABC patients have been studied: one group was randomly given anthracycline based neoadjuvant chemotherapy treatment and the other was with the provision of primary radiotherapy, using p53 as an indicator. IHC was conducted based on Miller Payne criteria and also noted size of residual tumor burden and type of tumor mass reduction (shrinkage or shattered) to determine change in ER, PR, Her2 neu expression.

Results: 87.50% and 40.62% of local control areas were obtained from radiotherapy and chemotherapy LABC patients. Chi-square analysis with continuity correction result was $p < 0.05$ and RR = 3.927, therefore radiotherapy is predicted to have significant contribution to local control effect. In contrary, p53 expression results was demonstrated non significantly result in response to anthracycline based neoadjuvant chemotherapy and radiotherapy local control effect, as low as $p = 0.150$ and $p = 1.00$, respectively. However. RR was achieved in p53 wild type for anthracycline based neoadjuvant chemotherapy, accounted for 2.250, while in radiotherapy was 1.000. The immunohistochemical expression of HER-2/neu and estrogen and progesteron receptors showed a weak correlation before and after neoadjuvant chemotherapy treatment (HER-2/neu, rho = 0.34; $P = 0.0009$; $k = 0.35$ [95% CI, 0.19–0.51]).

Conclusion: In summary, radiotherapy is statistically showing a better local control effect than anthracycline-based neoadjuvant chemotherapy. P53 expression can be used as a predictor in achieving local control effect to respond to antracycline-based neoadjuvant chemotherapy but not in radiotherapy. However. IHC status showed no significant change on ER, PR and Her2/neu before and after treatment.

Disclosure of Interest: I declared that I don't have conflict of interest with the company or commercial enterprise.

P254

PREDICTIVE SIGNIFICANCE OF BREAST CANCER SUBTYPES IN RESPONSE TO NEOADJUVANT CHEMOTHERAPY

N. Kobayashi[1]*, Y. Kiriyama[2], M. Hikichi[3], S. Miyajima[1], M. Kuroda[2], T. Utsumi[1]. [1]*Breast Surgery, Fujita health university, Toyoake, Aichi, Japan,* [2]*Pathology, Fujita health university, Toyoake, Aichi, Japan,* [3]*Brest Surgery, Fujita health university, Toyoake, Aichi, Japan*

Goals: Recent studies have shown that new molecular classification of breast cancer has important prognostic value and therapeutic implications. The aim of this study was to examine the predictive role of breast cancer subtypes in response to neoadjuvant chemotherapy (NAC).

Methods: We retrospectively reviewed the clinical and pathologic data of patients with breast cancer who received NAC from January 2005 to December 2011. Patients with HER2 negative tumors were treated with 4-cycle anthracycline-containing chemotherapy followed by 4-cycle taxan and those with HER2 positive tumors were treated with 4-cycle anthracycline-containing chemotherapy followed by 4-cycle taxan concomitant trastuzumab. The expression of Ki-67 was assessed by immunohistochemistry with a monoclonal MIB1 antibody. Ki-67 labeling index was categorized as low (<14%) and high (≥15%) in IBC. Tumors were classified as luminal A (ER+ and/or PR+, and HER2− and Ki-67 low), luminal B (ER+ and/or PR+, and HER2+ or Ki-67 high), HER2 disease (ER−, PR−, HER2+), or triple negative (ER−, PR−, HER2−). Pathological complete response (pCR) was defined as no invasive and no in situ residuals in breast at the time of surgery.

Results: Among 150 patients, a pCR was seen in 29 (19.3%) patients. The Number of patients in each subtype was as follows; luminal A 50 patients (33.3%), luminal B 48 patients (31.3%), HER2 disease 11 patients (8.0%), and triple negative 41 patients (27.3%). The median age in each group was 49, 48, 52, and 58 years old, respectively. The median tumor size was 3.3 cm, 3.5 cm, 3.1 cm, and 3.5 cm, respectively. pCR rates according to different subtypes were as follows: luminal A, 3 of 50 (6.0%), luminal B, 8 of 48 (16.7%), HER2 disease, 5 of 11 (45.5%), and triple negative, 13 of 41 (31.7%) ($p = 0.002$). ER negative, PgR negative, high Ki-67, and high histological grade were also the significant predictive factors for pCR ($p = 0.001$, 0.028, 0.014, and 0.004, respectively).

Conclusion: Our study suggests that immunohistochemical subtypes are good predictors for response to NAC in breast cancer patients.

Disclosure of Interest: No significant relationships.

P255

RESPONSE TO NEOADJUVANT CHEMOTHERAPY AND PROGNOSIS OF BREAST CANCER ACCORDING TO INTRINSIC SUBTYPE

M. Kochi[1] *, Y. Kajiwara[2], M. Kouno[3], M. Ito[2], S. Ohtani[2], K. Higaki[1]. [1]*Department of Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan,* [2]*Department of Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan,* [3]*Department of Oncology, Hiroshima City Hospital, Hiroshima, Japan*

Goals: Response to neoadjuvant chemotherapy of primary breast cancer differs across intrinsic subtypes and is considered as a useful surrogate indicator for prognostic prediction, while some subtype populations seems to take different course. We therefore examined response to neoadjuvant chemotherapy and prognosis according to intrinsic subtype.

Methods: We classified 441 primary breast cancer patients, who received neoadjuvant chemotherapy between 2002 and 2011 at our institute, to 5 intrinsic subtype groups; Luminal A type (LA), Luminal B type (LB), Luminal Her2 type (LH), Her2 type (Her2) and triple negative (TN) groups, according to hormonal sensitivity, Her2 status, and cancer proliferation, and examined their pathological response to neoadjuvant chemotherapy and prognosis. Pathological complete response (pCR) is defined as necrosis or disappearance of invasive cancer of breast and axillary lymph node metastases, approving residual non-invasive component of breast. We also examined disease free survival (DFS) and overall survival (OS) by each subtype statistically, using Kaplan–Meier method and Log-rank test.

Results: Number of patients in each subtype were as follows; LA: 148 (33.6%), LB: 68 (15.4%), LH: 45 (10.2%), Her2: 71 (15.8%), and TN: 109 (24.7%). Surveillance period was 4–124 months (median: 29 months). Most of cases in all subtypes received both anthracycline and taxane based treatment. 34 cases in LH (75.6%) and 65 cases in Her2 (91.5%) were treated with trastzumab. pCR rate in each subtype groups were as follows; LA 19.9%, LB 4.7%, LH 22.2%, Her2 54.9%, TN 28.4%. pCR rate was significantly high in Her2 and TN ($p < 0.05$). Luminal types showed no significant differences in DFS and OS between pCR group and non-pCR group. (LA and LB; DFS $p = 0.910$ OS $p = 0.782$, LH; DFS $p = 0.465$ OS $p = 0.691$). In Her2, pCR group showed significantly better prognosis compared to non-pCR group. (DFS $p = 0.014$, OS $p = 0.046$). In TN, DFS was significantly better in pCR group, while OS tended to be better in pCR groups but not significant (DFS $p = 0.0026$, OS $p = 0.066$).

Conclusion: Our results may indicate the correlation between response to neoadjuvant chemotherapy and prognosis in Her2 and TN breast cancer.

Disclosure of Interest: No significant relationships.

P256

EFFICACY OF HER2-TARGETED THERAPY FOR HER2 POSITIVE BREAST CANCER ACCORDING TO HR STATUS

T. Murata[1] *, M. Takahashi[2], T. Hayashida[1], S. Hirose[3], H. Jinno[2], Y. Kitagawa[4]. [1]*Surgery, Keio University School of Medicine, Tokyo, Japan,* [2]*Department of Surgery, Keio University School of Medicine, Tokyo, Japan,* [3]*Pathology, Keio University School of Medicine, Tokyo, Japan,* [4]*General and Gastrointestinal Surgery, Keio University School of Medicine, Tokyo, Japan*

Goals: Hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-positive tumors generally cluster within the luminal/HER2 subset; whereas HR-negative/HER2-positive tumors reside in HER2-enriched subset. We investigated whether the efficacy of HER2-targeted therapy for HER2-positive tumors differs by HR status.

Methods: Forty-five patients with operable breast cancer received 12 cycles of weekly paclitaxel (80 mg/m^2 IV) plus weekly trastuzumab (4mg/kg loading dose followed by 2 mg/kg IV) before surgery at Keio University Hospital from March 2009 to December 2012. All tumors were HER2-positive by immunohistochemistry (IHC) or fluorescence in situ hybridization. Expressions of ER, PgR and Ki67 were performed by IHC in core needle biopsy samples at baseline. ER and PgR status was assessed using Allred score. For Ki67 labeling index, a total of 400 cells were counted from three consecutive high-power magnifications. Pathological complete response (pCR) defined as no invasive residuals in breast. All patients with luminal/HER2 tumors received adjuvant endocrine therapy in addition to adjuvant trastuzumab monothereapy.

Results: Forty-five patients with HER2-positive tumors were divided into 20 (44.4%) patients with luminal/HER2 tumors and 25 (55.6%) patients with HER2-enriched tumors, respectively. There were no significant differences in age, tumor size, clinical nodal status, nuclear grade, and Ki67 status between the two groups (median age (range): 52 (35–78) vs. 61 (31–72), $p = 0.096$, mean tumor size: 3.01 ± 1.42 cm vs. 3.53 ± 2.22 cm, $p = 0.354$, clinical node positive rate: 50.0% vs. 32.0%, $p = 0.241$, nuclear grade 3 rate: 43.8% vs. 59.1%, $p = 0.512$, mean Ki67 score: 40.6% vs. 39.2%, $p = 0.848$, respectively). Clinical complete response (cCR) rate and objective response rate (ORR) were similar between the two groups (cCR: 50.0% vs. 52.0%, $p = 1.000$, ORR: 85.0% vs. 88.0%, $p = 1.000$). Breast conserving surgery was performed in 85.0% of patients with luminal/HER2 tumors and 84.0% of patients with HER2-enriched tumors ($p = 1.000$). Compared to patients with luminal/HER2 tumors, patients with HER2-enriched tumors had significantly higher pathological complete response rate (40.0% vs. 72.0%, $p = 0.039$). 8 patients with luminal/HER2 tumors and 11 patients with HER2-enriched tumors were treated with four cycles of epirubicin/cyclophosphamide/fluorouracil as adjuvant chemotherapy. With 26 months median follow-up, no significant differences were observed between the two groups with respect to disease-free survival. Estimated 2-year disease-free survival for luminal/HER2 and HER2-enriched was 93.3% and 100.0%, respectively ($p = 1.000$).

Conclusion: HER2-enriched breast cancer showed significantly higher pathologic complete response rate to HER2-targeted therapy compared with luminal/HER2 breast cancer. However, there was no significant difference in disease-free survival between the two groups.

Disclosure of Interest: No significant relationships.

P257

EFFICACY AND IMPACT OF WEEKLY PACLITAXEL IN BREAST CANCER NEOADJUVANT TREATMENT IN ARGENTINA

M.I. Bianconi[1] *, S. Otero[1], P. Saldias[1], A. Parcero[1], C. Storino[2], G. Jankilevich[1]. [1]*Oncology, Hospital Carlos G Durand, Buenos Aires, Argentina,* [2]*Obstetric and Gynecology, Hospital Carlos G Durand, Buenos Aires, Argentina*

Goals: The introduction of taxanes in the neoadjuvant setting became standard in the last decade. We compare efficacy in two ages, taxane and pre taxane age.

Methods: Consecutive patients (pts) with breast cancer diagnosis and neoadjuvant treatment were treated in our hospital. We checked medical records and compared complete reponse and treatment duration between period 1 (pre w taxane age) 1995–2009 and period 2 (w taxane age) between 2009–2012.

Results: 120 pts were recorded. 76 pts in period 1 and 35 period 2. Median age XX years. Complete response (period 1 vs 2) p 0.0017, impact of time duration (period 1 vs 2) $p = 0.04$, breast-conservation rate period 1 13% period 2 74% The compliance was 98%, and all pts with low resources had accessibility to drugs and complete the treatment.

Conclusion: High percentage of complete response and long duration of treatment are linked with weekly paclitaxel use.

Disclosure of Interest: No significant relationships.

P258

EVALUATION OF TUMOR RESPONSE TO NEOADJUVANT CHEMOTHERAPY BY FUNCTIONAL IMAGING TECHNOLOGIES

M. Gonzalez Cao[1]*, M. Simo[2], B. Ubeda[3], F. Treserras[4], C. Ara[2], J. Brown[3], R. Fabregas[5], S. Baulies[5], A. Martinez[1], M. Cusido[3]. *[1]Medical Oncology, Institut Universitari Dexeus, IOR, Barcelona, Spain, [2]Nuclear Medicine, Institut Universitari Dexeus, Barcelona, Spain, [3]Ginecology Department, Institut Universitari Dexeus, Barcelona, Spain, [4]Institut Universitari Dexeus, Barcelona, Spain, [5]Gynaecology, Dexeus University Institute, Barcelona, Spain*

Goals: Aims Current methods for tumor response evaluation during neoadjuvant chemotherapy in breast cancer, have shown limited success. Functional imaging technologies as FDG-PET and MRI have been evaluated in this study.

Methods: Methods FDG-PET and MRI were performed in 26 breast cancer patients treated with six months of neoadjuvant chemotherapy. Tumor evaluation was performed pretreatment, after the first three months of chemotherapy and when chemotherapy treatment was completed, previous to the surgical treatment. Pathologic response was evaluated by Miller-Payne classification.

Results: Results Median age was 46 (39–70). Thirteen patients had positive hormonal receptors and 6 patients were erb-2 positive. Ten patients achieved a complete pathological response (pCR). Relative decrease in FDG uptake after 3 months of chemotherapy was greater in patients that had a pCR (97% vs 61%, p 0.030). Delta SUV <−70% after three months of treatment, predicted pCR with an accuracy of 87%. The absolute value of SUVmax pretreatment, was not predictive of pCR, because some patients with low SUVmax achieved a pCR and not all patients with tumors with high values of SUVmax had a completed pathologic response: median SUV max in patients with pCR was 5 (2–24), versus 6 (3.4–16). Decrease of tumor size greater than 40%, after three months of chemotherapy, was correlated with pCR (67% vs 33%). In patients with pCR, changes in size by MRI were −60% versus −21% (p = 0.051) in patients without pathologic response.

Conclusion: Conclusions Tumor response evaluation by FDG-PET and MRI is correlated with pathologic response in breast cancer patients treated with neoadjuvant chemotherapy. Updated results and correlation between these two methods will be presented during the meeting.

Disclosure of Interest: No significant relationships.

Locally advanced and metastatic disease

P260

CTC IN PREDICTING THE EFFICACY OF NEOADJUVANT CHEMOTHERAPY IN LABC PATIENTS: A META-ANALYSIS

F. Fei*, Y. Du, G. Di, J. Lu, J. Wu, Z. Shao. *Breast Surgery, Shanghai Cancer Center Fudan University, Shanghai, China*

Goals: Circulating tumor cell (CTC) is not only a proliferation marker of tumor cells, but also a prognostic biomarker and predictive factor. We aim to evaluate the association between the sensitivity of CTCs and the efficacy of neoadjuvant chemotherapy for local advanced breast cancer (LABC) patients.

Methods: PubMed, EBSCO, Web of Science, conference proceedings and key trials are searched from 1998 to 2012. The hazard ratio (HR) is used to evaluate the ability of CTC to predict the efficacy of the neoadjuvant chemotherapy in local advanced breast cancer patients. All of the data from each study use either fixed-effects or random-effects by Stata.

Results: There is no between-study heterogeneity in DFS (heterogeneity $\chi^2 = 0.02$ (d.f. = 1), I2 = 0.0%, P = 0.877). Our meta-analysis find that the decreased CTC number in LABC patients after neoadjuvant chemotherapy is not associated with PCR in the pathological response. (HR = 0.918, 95% CI: 0.650–1.295; P = 0.877).

Conclusion: The results of the current meta-analysis support this hypothesis and indicate no association between clinical benefits and the decrease of CTC number. According to our result, LABC patients are not probably led to better clinical benefit although their CTCs decrease after NT. Due to the limitation, more randomized clinical trials are needed to confirm the conclusion.

Disclosure of Interest: No significant relationships.

P261

OLIGOMETASTATIC BREAST CANCER: A SINGLE INSTITUTION EXPERIENCE

C.M. Kelly[1]*, C. Brady[2], E. Moylan[1], S. O'Reilly[2]. *[1]Medical Oncology, Cork University Hospital, Cork, Ireland, [2]Medical Oncology, Mercy University Hospital, Cork, Ireland*

Goals: A subset of stage IV breast cancer represents oligometastatic disease (OMBC), characterised by solitary or few detectable metastases. An aggressive multidisciplinary therapeutic approach is recommended. The objective of this study is to determine the number of patients with OMBC treated with this approach and the number remaining in a complete remission (CR).

Methods: Clinical, pathological, management and outcome data were collected retrospectively on patients with OMBC treated at our institution over the last 30 years. OMBC was defined as: 1 or 2 organs involved with metastatic lesions (excluding the primary breast lesion resectable by surgery), fewer than 5 lesions per metastasized organ and lesion diameter less than 5 cm.

Results: 23 patients were identified. The mean age at diagnosis was 49 years (30–71). For three individuals OMBC represented the initial diagnosis. Of the remainder, the average time to disease recurrence was 4.4 years. Metastatic disease was confined to 1 organ in 96% (n = 22) whilst one patient had disease involving 2 organs. The most common sites of metastasis included: brain (n = 13, 57%) and bone (n = 7, 30%). One individual had lung and lymph node involvement, one liver involvement and one soft tissue involvement. With regards to pathologic prognostic markers 39% were ER positive, 35% were PR positive and 44% were Her2neu amplified. Definitive surgery on the primary breast mass was undertaken in the majority (n = 22, 96%) with 74% having a mastectomy and the remainder breast conserving surgery. An aggressive curative strategy was delivered to 75% (n = 15) of patients. Of those with OMBC to brain (n = 13, 57%) the therapeutic strategy included: definitive surgical resection (n = 10, 77%), whole brain radiotherapy (n = 12, 92%), chemotherapy (n = 2, 15%), and hormone therapy (n = 2, 15%). In the case of metastasis to bone: radiotherapy was delivered to 5 patients [radical (n = 4), palliative (n = 1)], chemotherapy was given to 1 patient (14%) and hormone therapy to 6 patients (86%). One patient with liver involvement received neoadjuvant chemotherapy prior to definitive liver resection. The patient with OMBC to lung and lymph nodes achieved a CR with chemotherapy alone. With regards to outcome the survival data is as follows: 30% are alive without evidence of disease, 16% are alive with stable disease, 9% are alive with new areas of disease and 30% are dead due to breast cancer. Of those treated with curative intent 40% (n = 6, 6/15) remain in a CR.

Conclusion: An aggressive multidisciplinary approach can result in complete resolution of OMBC in a reasonable number of patients.

Disclosure of Interest: I have no disclosures.

P262

LAPATINIB IN EGYPTIAN METASTATIC CANCER WOMEN: IN WHICH DOSE AND FREQUENCY?

N.A.R. Ahmed*, R.A. Malek, O.A. Rahman, M. Magdy, H.A. Azim. *Oncology, Kasr alainy hospital, Cairo, Egypt*

Goals: Lapatinib is a small-molecule kinase inhibitor that targets the epidermal growth factor receptor and the human epidermal

growth factor receptor 2 (HER2). In March 2007, lapatinib distosylate monohydrate (Tykerb; GlaxoSmithKline) was approved by the FDA for the treatment of patients with advanced or metastatic breast cancer whose tumours overexpress HER2 and who have received prior therapy including an anthracycline, a taxane and trastuzumab. In phase I–II studies that published in American society of clinical oncology 2005, lapatinib was well tolerated at doses ranges from 650–1600 mg in heavily pretreated patients with ErB1-expressing and/or ErB2 overexpressing metastatic solid tumors. At doses where clinical activity was observed, drug related toxicity was primarily restricted to GI-II diarrhea (42%) and skin rash (31%).

Purpose: This study determined the range of effective tolerable doses of lapatinib in Egyptian population with metastatic breast (BC) cancer, considering the progression free survival the end point.

Methods: 27 egyptian femals with ErB2-positive metastatic BC were treated at Cairo oncology center from 2008–2012 received orally daily doses ranges from 750 mg (2+1), and 1000 mg (2+2), regardless fasting condition. (16 of 27, 59.2%) treated with lapatinib plus chemotherapy, and (12 of 27, 44.4%), (7) patients received 750 mg, while (20) received 1000 mg.

Results: The median age of patients was 49.5 years. The majority of drug-related adverse events was mild (Grade 1–2), the most common events were Skin rash and mucositis (7 of 27; 25.9%), (4 of 27; 14.8%), No Grade 4 adverse event was observed. There were Grade 3 drug-related adverse events in five patients (3 of 5 skin toxicities, 2 of them diarrhea). The median progression free survival for whole group was 5.55 which is not significant for factor affecting free survival.

Conclusion: Lapatinib was well tolerated at doses of 750–1000 mg/day in Egyptian solid tumor patients. Overall, our findings were similar to those of overseas studies. Further studies must be obtained regarding the pharmacokinetics of lapatinib and the administration time with or without food.

Disclosure of Interest: No significant relationships.

P263
DOES PALLIATIVE SURGERY TO THE BREAST IMPROVE OUTCOME OF PATIENTS WITH METASTATIC T4 BREAST CANCER?

S. Arifi[1] *, F. Hijri[2], Z. Benbrahim[2], N. Mellas[2], A. Banani[3], M.A. Malhouf[3], O. El Mesbahi[2]. *[1]Medical Oncology, Hassan II University Hospital, Fez, Morocco, [2]Medical Oncology, Hassan II University Hospital, Fez, Morocco, [3]Gynecology, Hassani II University Hospital, Fez, Morocco*

Goals: Women with metastatic breast cancer (MBC) with intact locally advanced primary tumors (LAT) present aggressive local symptoms that may warrant palliative surgery to the breast. However, it is unclear if such surgery otherwise improves clinical outcome. The aim of this study is to demonstrate if surgery of the breast may avoid uncontrolled chest wall disease and may improve survival.

Methods: We reviewed the records of all MBC patients presented with intact LAT, treated at our institution between 2007 and 2011. We compared two groups of patients: surgical group versus nonsurgical group. Clinical outcome was assessed in the two groups. Prognostic factors affecting loco regional relapse were evaluated.

Results: 75 patients were identified. The mean patient age was 49±12.15 years. 52% were pre menopausal women. 87.1% of tumors were hormone receptors (HR) positive. Her2 was assessed in 59 cases and was positive in 33.9%. Inflammatory breast cancer presented 16%. Clinical lymph node involvement was noted in 58.7% cases. 69.6% had visceral metastasis and 5.3% had brain metastasis. 89.3% were PS ≤ 1. All women received systemic therapy. First-line therapy consisted of anthracycline-based regimen (95.6%) and Taxane (39.7%). Among patients with HER2 positive 36.4% received Trastuzumab. Only 14% of patients with bone metastasis received bisphosphonate. 49.3% underwent mastectomy while 50.7% had intact LAT. The two groups were well balanced regarding demographics, clinicals and tumors characteristics. Among women who underwent mastectomy 48.5% had axillary lymph node dissection, and excision margins were positive in 25% cases. Loco regional radiotherapy (LRRT) was given to 8 women. pCR occurred in 7 patients among those who were operated.

Local recurrence (LR) occurred in 9 patients (28.1%). Median time to local relapse was 3 months (2–19). LR was related to excision margin ($p = 0.0001$) and LRRT ($p = 0.04$). Median PFS was 10 months in nonsurgical group patients versus 16.5 months in surgical group.

Conclusion: Stage IV patients with locally advanced breast cancer who underwent mastectomy had improvement in local symptoms when the excision margin are in sano. However, the impact of this surgery in survival is not clear.

Disclosure of Interest: No significant relationships.

P264
Abstract withdrawn

P265
TRASTUZUMAB WITH CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

A. Alsayed[1] *, H. Alhashem[2], M. Almashaikhi[1], S. Alhayli[1], M. Sajjad[3], T. Twegieri[2], K. Suleman[1], T. Elhassan[1], D. Ajarim[1]. *[1]Department of Oncology, King Fasial Specialist Hospital and Research Center, Riyadh, Saudi Arabia, [2]Oncology, King Faisal Hosp and RC, Riyadh, Saudi Arabia, [3]Oncology, King Fahad Sp Hospital, Dammam, Saudi Arabia*

Goals:
- Assess the pCR in locally advanced breast cancer (LABC) undergoing Trastuzumab (T) with chemotherapy (CT)
- Study factors associated with pathological complete response (pCR)
- Determine the disease free (DFS) and overall survival (OS)

Methods: LABC staged 2 and above undergoing upfront T and CT who underwent surgery from June 2005-Feb 2011 using our database were reviewed. All pts had adjuvant radiation and T. Hormonal therapy if hormone receptor (HR) positive. Pts had to have an IHC stain of + 3 for Her2 neu or positive Fluorescent in situ hybridization FISH or both. We identified 98 cases. Statistical analysis performed using SPSS version 20. Chi square test and Carmar V coefficient was used in order to evaluate the association between pCR in breast and axilla, with factors including menopausal status, age, histology grade, (HR) status clinical stage and type of chemotherapy. pCR in the breast was defined as DCIS or having no residual invasive disease. PCR response in the axilla was absence of carcinoma cells by IHC Pts were divided into 2 subgroups regarding the CT type either Anthracycline (A) or non Anthracycline (NA) CT. For group A, T was used sequentially Pts were followed for DFS and OS Stage 4 patient with LABC undergoing surgery were included only in the assessment of pathological response.

Results: The median age was 44 years and the majority of the pts were premenopausal and all pts had invasive ductal cancer IDC. Median follow up was 36 (13–74) months. The stage were as follows stage II 12%, stage III 59% while 26% had stage IV disease. 97 pts underwent surgery. The rate of pCR was 50% in the breast, 51% in axilla and 37.8% in breast and axilla. The rate of pCR in the breast and axilla was 67%, 38% and 24% in stage II, III and IV respectively. pCR was correlated with clinical stage while no correlation was seen with the age, menopausal status, HR status or grade of tumor. The Chi square test revealed a significant association between pCR in breast and axilla with the clinical stage, $p = 0.03$. Logistic regression showed that pts with stage II are more likely to achieve pCR in breast and axilla in comparison to stage IV patients, odds ratio 6.3, 95% CI 1.3–28, $p = 0.01$. Pts with stage III have higher chance to achieve pCR in breast and axilla when compared to stage IV, but did not

reach statistical significance. Sixty-five percent of patient had A as part of their chemotherapy regimen. Forty five percent 28/62 of this group achieved pCR while 9 out of 33 (27%) in NA group achieved pCR. A trend was seen but this did not reach statistical significance. For the nonmetastatic patients five year DFS was 71% and OS 94%. DFS in pCR was 91% compared to 59% who did not achieve pCR (P = 0.008).

Conclusion: T with CT is efficacious in a group of LABC cancer and is associated with a high rate of pCR. Clinical stage correlates with pCR. A containing regimens have shown a non-significant trend towards higher pCR. pCR is associated with improved outcome in LABC undergoing T with CT similar to early breast cancer.

Disclosure of Interest: No significant relationships.

P266

INFLAMMATORY BREAST CANCER AND NON INFLAMMATORY LOCALLY ADVANCED BREAST CANCER: A DISTINCT ENTITY

Z. Benbrahim[1] *, S. Arifi[1], S. Chahbouni[2], K. Daoudi[1], S. El Fakir[3], C. Nejjari[3], A. Amarti[2], N. Mellas[1], O. El Mesbahi[1]. *[1]Medical Oncology, Hassan II University Hospital, Fez, Morocco, [2]Pathology Department, Hassan II University Hospital, Fez, Morocco, [3]Epidemiology, Faculty of medicine and pharmacy of Fez, Fez, Morocco*

Goals: Background: Inflammatory breast bancer accounts of 7% of all invasive breast tumors in Morocco. It is associated, as locally advanced non inflammatory breast cancer, with poor prognosis. However, whether they are distinct clinic-pathologic entities remains controversial.

Objectives of the study: To compare clinico-pathologic features, clinical and pathological response to neoadjuvant chemotherapy and progression free survival (PFS) and overall survival (OS) of inflammatory breast cancer (IBC) and non inflammatory locally advanced breast cancer (LABC) in Morocco.

Methods: We reviewed retrospectively 90 cases of locally advanced non metastatic breast cancer treated with neoadjuvant chemotherapy between January 2009 to June 2012 in the Medical Oncology Department at Hassan II University Hospital. Clinical, histopathologic and prognostic features of these two entities were evaluated. The Kaplan–Meier method and Log Rang test were used to estimate and compare the overall and disease free survival among groups.

Results: Thirty five patients were IBC and 55 were LABC. The mean patient age was 46.5±9.5 years (44.8 in IBC vs. 47.6 in LABC; p = 0.1). Premenopausal status at diagnosis was frequently noted in IBC (71.4% vs. 45.5%; p = 0.01). The mean of tumor size was highest in IBC (10.3 vs. 6.8 cm; p = 0.01). Clinical lymph node involvement was noted in 65.7% in IBC vs. 40% in LABC (p = 0.09). Poorer tumor grade (50% vs. 23.6%; p = 0.01), high MIB-1 score (66.7 vs. 33.3%; p = 0.002) and presence of vascular invasion (37.5 vs. 17.6%; p = 0.03) were more predictive of IBC than of LABC. The two groups were well balanced regarding hormonal receptors and Her2 positivity. There were a no statistically significant lower clinical and pathological complete response to neo-adjuvant chemotherapy in the IBC as compared with LABC patients [(6.1% vs. 18.5%; p = 0.1) and (8.7% vs. 11.6% p = 0.7), respectively]. After a median follow-up of 18 months (range: 5–48 months), the medians of PFS and OS were shorter in IBC than LABC (6 vs. 14 months; p < 0.003) and (14 vs. 24 months; p < 0.05) respectively.

Conclusion: IBC and LABC are distinct clinical and biological entities with different prognostic profiles. Confirmation of these finding in a larger prospective cohort will emphasize the need for different management approaches for these two distinct entities.

Disclosure of Interest: No significant relationships.

P267

TREATMENT STRATEGY FOR LATE RECURRENCES IN BREAST CANCER PATIENTS

S. Hayama *, R. Nakamura, N. Yamamoto. *Breast Surgery, Chiba Cancer Center Hospital, Chiba city, Chiba, Japan*

Goals: Patients with breast cancer diagnosed at an early stage with small tumors and no lymph node metastasis may show a high rate of recurrence when followed for more than 5 to 10 years.

It is important in the therapy of patients with late recurrence of breast cancer to consider the clinical factors at the time of the recurrence and the pathological features of the metastases.

The aim of this study was to investigate the prognostic factors in patients with late recurrence of breast cancer.

Methods: We conducted a retrospective review of 5516 patients who had undergone surgery at our institute for primary breast cancer between 1980 and 2010.

Of these patients, 112 patients (2%) developed recurrence between 5 and 10 years after the primary surgery.

We considered whether any pathologic factors might be correlated with the prognosis.

We evaluated whether the pathological factors at the time of the primary operation, an opportunity of recurrent finding, metastatic sites and a recurrent initial treatment were correlated with a prognosis.

Results: The 10-year overall survival rates (10ys-OS) after recurrence in cases with an ER(+) status and ER(−) status of the primary tumor were 16.2% and 11.5% (P < 0.05), respectively.

The 10ys-OS in patients with and without visceral metastases (liver, lung, pleura, peritoneum) at the time of the initial recurrence were 37.4% and 12.5% (P < 0.05) respectively. While, there is no significant difference to 10ys-OS in tumor diameter at the primary operation, in the presence or absence of lymph node metastases, and in the presence or absence of symptom at recurrent findings.

There was no significant difference in the 10ys-OS in the ER(+) patients between the group treated by chemotherapy and the group treated by endocrine therapy as the initial treatment for recurrence.

Furthermore, the 10ys-OS in the group in which the endocrine therapy could be continued for more than 6 months for the first recurrence, and the group in which the endocrine therapy needed to be switched to chemotherapy within 6 months were 22.8% and 0%, respectively (P < 0.05). The concordance rates in regard to ER and HER2 over expression between the metastatic lesion and the primary tumor were 66.7% and 83.3%, respectively. There was no significant difference in the OS between patients who underwent/did not undergo biopsy for confirmation of the HER2 over expression and ER expression status of the recurrent lesions among breast cancer patients.

Conclusion: The prognosis of breast cancer patients with ER(+) late relapse was superior as compared with that of the breast cancer patients with ER(−) late relapse.

The prognosis was poor in patients in whom the endocrine therapy for the first relapse could not be continued for more than 6 months.

The discordances in the tumor characteristics between primary and metastatic breast cancer were, therefore, not associated with any detrimental effects on the outcomes.

Disclosure of Interest: No significant relationships.

P268

PHASE I/IIB CLINICAL TRIAL COMPARING PK AND SAFETY OF TRASTUZUMAB AND ITS BIOSIMILAR CANDIDATE CT-P6

Y. Im[1] *, D. Krasnozhon[2], I. Bondarenko[3], Z. Zvirbule[4], K. Jung[5], P. Oliynychenko[6], M.H. Lee[7], S. Im[8], H.U. Kim[9], S. Tjulandin[10], J.S. Ro[11], O. Burdaeva[12], S. Lee[13], S. Radulovic[14], J. Nedovic[15]. *[1]Department of Medicine, Samsung Medical Center, Seoul, South Korea, 2. GUZ Leningrad Regional Oncological Dispensary, St Petersburg, Russian Federation, [3]State Medical Academy, Dneproetrovsk, Ukraine, [4]Latvian Oncology Center, Riga, Latvia, [5]Asan Medical Center, Seoul, South Korea, [6]City Oncology Hospital, Kiev, Ukraine, [7]Inha University Hospital, Incheon, South Korea, [8]Seoul National University Hospital, Seoul, South Korea, [9]CELLTRION Inc, Incheon, South Korea, [10]RAMS Russian Oncology Research Center, Moscow, Russian Federation, [11]Center For Breast Cancer, National Cancer Center, Goyang, South Korea, [12]Institute Siberian Branch of Russian Academy of Medical Sciences, Novosibirsk, Russian Federation, [13]Internal Medicine, Dong-A University Medical Center, Busan, South Korea, [14]Institute of Oncology and Radiology of Serbia, Beograd, Serbia, [15]Clinical Center Kragujevac, Kragujevac, Serbia*

Goals: This Phase I/IIb study compared the pharmacokinetics (PK) and safety of trastuzumab and CT-P6, a biosimilar to trastuzumab, in women with HER2+ metastatic breast cancer (MBC).

Methods: In this double blind, randomized, parallel-group study, 174 patients with HER2+ MBC were randomized 1:1 to receive either CT-P6 (n = 86) or trastuzumab (n = 88) 8 mg/kg intravenously (day 1), followed by CT-P6 or trastuzumab 6 mg/kg every 3 weeks. Paclitaxel (175 mg/m^2 3-weekly) was co-administered. The primary endpoint, area under the concentration-time curve at steady state (AUC_{SS}), was measured during treatment cycle 8, although treatment was continued until disease progression, death or patient withdrawal. Serum blood samples for PK analysis were obtained immediately prior to the study treatment infusion and at the end of the study treatment infusion on dosing days. For primary PK analysis, a total of 10 serum blood samples were obtained during cycle 8. Patients were monitored for safety and tolerability throughout the study.

Results: Primary PK analysis was performed in 100 patients who reached steady state. Geometric mean AUC_{SS} (% coefficient of variation [%CV]) was 32,000 μgh/mL (43.5%) for CT-P6 and 30,600 μgh/mL (30.9%) for trastuzumab. The ratio of geometric means was 104.57% (90% CI: 93.64, 116.78) for AUC_{SS}. The limits of the 90% CIs for the ratio of AUC_{SS} geometric means were contained within the established margin (80–125%) required for bioequivalence. Geometric mean $C_{troughSS}$ was 19.5 μg/mL for CT-P6 and 19.2 μg/mL for trastuzumab. The ratio of geometric means was 101.35% (90% CI: 87.94, 116.82) for $C_{troughSS}$. PK parameters including C_{max}, C_{min}, C_{av}, T_{max}, CL, V_Z, MRT, PTF and $T_{1/2}$ were not different in CT-P6 and trastuzumab. Serious adverse events (SAEs) were reported in 15.8% of CT-P6 and 20.9% of trastuzumab patients; 2.6% and 3.0% were treatment-related, respectively. Overall, treatment-related AEs were reported in 40.8% of CT-P6 and 46.3% of trastuzumab patients. Hypersensitivity, infusion reaction, cardiotoxicity, and infection (any grade) were reported in 1.3%, 19.7%, 2.6% and 1.3% of CT-P6 and 1.5%, 35.8%, 7.5% and 0% of trastuzumab patients, respectively.

Conclusion: CT-P6 and trastuzumab were equivalent for AUC_{SS} in patients with HER2+ MBC. $C_{troughSS}$ and other PK parameters further confirmed CT-P6 and trastuzumab comparability. CT-P6 was well tolerated, with a safety profile comparable to that of trastuzumab.

Disclosure of Interest: All authors have received research funding, and/or travel support directly related to this clinical trial from Celltrion Inc.

P269

BASELINE STAGING TESTS FOR LOCALLY ADVANCED BREAST CANCER

R.A.C. Vieira[1] *, G.F. Garcia[1], A.G. Zucca-Matthes[1], G. Uemura[2], M.M. Brentani[3], M.A.A.K. Folgueira[3]. *[1]Mastology and Breast Reconstruction, Barretos Cancer Hospital, Barretos – SP, Brazil, [2]Gynecology, Obstetrics and Mastology, Botucatu School of Medicine, Botucatu, Brazil, [3]Radiologia, Disciplina de Oncologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo/Brazil*

Goals: To evaluate the impact of different radiological exams in the clinical staging of locally advanced breast cancer (LABC) and the possibility to evaluate bone metastasis with computed tomography (CT) in substitution of scintigraphy.

Methods: A prospective clinical trial (www.clinicaltrials.gov; NCT00820690) performed in breast cancer women during 06/2008 to 05/2011. Patients with invasive carcinoma, clinical stage III, absence of systemic symptoms and absence of previous treatment were included. Exclusion criteria were the absence of invasive disease, staging exams and follow-up. The patients were submitted to a clinical examination, mammography, breast ultrasound and biopsy. To evaluate the presence of metastatic disease the patients were submitted to chest X-Ray, abdominal ultrasound, bone scintigraphy (conventional exams) and CT (abdominal and thoracic). In the presence of suspicion exams, complementary exams were performed. If the CT needs control, new exams were performed. All patients were submitted to neoadjuvant or palliative chemotherapy. At the end of study one radiologist reviewed all exams and medical reports. We evaluated the frequency of metastasis in the conventional exams and when the patients were evaluated with CT.

Results: 148 patients were enrolled, but 10 patients were excluded. From the 138 patients, the median tumor size was 6.6 cm (3–15 cm). Evaluating the clinical stage (TNM) there were 60.9% cT3, 38.4% cT4, 67.4% cN1, 25.4% cN2 and 2.2% cN3. After all exams performed 38 (28.3%) had metastatic disease. When we use conventional exams 8.7% had metastatic disease, but 17.4% needed complementary exams, leading to 13.8% [IC=8.08–19.55] of metastatic disease. When we use CT (abdominal and thoracic) and scintigraphy for staging, 28.3% [IC=20.8–34.9] had metastatic disease, with an increase of 14.5% of diagnosis of metastatic disease. The CT showed 6 patients (4.3%) with bone metastasis and normal scintigraphy, but it did not increased the frequency of metastatic disease.

Conclusion: Patients with LABC must be evaluated with a minimum of CT (abdominal and thoracic) added to the bone scintigraphy. The conventional exams decreased 14.5% of the metastatic disease diagnosis and the CT increased 4.3% of diagnosis of bone metastasis.

Disclosure of Interest: No significant relationships.

P270

POSSIBILITY FOR IPSILATERAL BREAST TUMOR RECURRENCE FOLLOWING BREAST CONSERVING SURGERY

Y. Kano[1] *, Y. Kajiwara[1], M. Kono[2], M. Kochi[1], M. Ito[1], S. Ohtani[1], K. Higaki[1]. *[1]Department of Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan, [2]Department of Oncology, Hiroshima City Hospital, Hiroshima, Japan*

Goals: Breast conserving surgery has already been established as a standard treatment for early breast cancer. And the standard treatment for ipsilateral breast tumor recurrence (IBTR) following breast conserving surgery might be a mastectomy. But there is not still sufficient evidence, therefore we need to evaluate the treatment options for IBTR following breast conserving operation.

Methods: We retrospectively analyzed 75 cases (2.9% of totally 3021 breast conserving surgeries) who have a IBTR following breast conserving surgery at our hospital between 1988 and 2011. Kaplan–Meier curves and log-rank tests were used to evaluate overall survival and relapse-free survival differences between lumpectomy and mastectomy for IBTR following breast conserving surgery.

Results: Of the 75 cases in whom repeat resection was performed, excluding who have inflammatory breast cancer, repeat lumpectomy was conducted in 37 cases and in the remaining 28 cases mastectomy was undertaken. Of the 37 cases who underwent lumpectomy, repeat IBTR developed in 7 cases. Of these 7 cases, lumpectomy was conducted in 2 cases, mastectomy in 4 cases and no resection in one distant metastasis case. Of the 28 cases who underwent mastectomy, repeat recurrence developed in 4 cases with distant metastasis. There were no statistically significant differences in overall survival (log-rank tests $p = 0.726$) or relapse-free survival (log-rank tests; $p = 0.315$) between the 2 treatments.
Conclusion: In view of these findings for IBTR, it is considered worthwhile to conduct repeat lumpectomy.
Disclosure of Interest: No significant relationships.

P271

PHASE 2 STUDY OF EVEROLIMUS PLUS LETROZOLE IN ER+ METASTATIC BREAST CANCER: BOLERO-4

F. Cardoso[1]*, T. Bachelot[2], W. Gradishar[3], S. Saletan[4], A. Graham[4], P. Liedke[5], S. Azevedo[5], V. Sriuranpong[6]. *[1]Breast Unit, Champalimaud Cancer Centre, Lisbon, Portugal, [2]Breast Cancer Unit, Centre Leon Berard, Lyon, France, [3]Feinberg School of Medicine, 3Northwestern University Medical School, Chicago, United States of America, [4]Novartis Pharmaceuticals Corporation, Novartis Pharmaceuticals Corporation, East Hanover, United States of America, [5]Oncologia E Tmo, Clinica de Hematoligia, Porto Alegre, Brazil, [6]Chulalongkorn University, Bangkok, Thailand*

Goals: The mammalian target of rapamycin (mTOR) pathway is an important regulator of tumor cell growth, metabolism, proliferation, and survival in breast cancer (BC). Evidence from previous clinical trials in the neoadjuvant and advanced hormone receptor-positive (HR+) BC settings showed that co-inhibition of the mTOR pathway using everolimus (EVE) and anti-estrogen therapy significantly improves treatment efficacy compared with endocrine therapy alone, both in patients without prior treatment and in those progressing after initial endocrine therapy (ET). In the phase 3 registration trial BOLERO-2, the combination of EVE + exemestane (EXE) led to a 5-month increase in progression-free survival (PFS) compared with EXE alone in postmenopausal women with HR+, human epidermal growth factor receptor-2 (HER2)-negative, advanced BC progressing after prior letrozole or anastrozole. The BOLERO-4 study will extend these investigations to evaluate the activity of EVE + letrozole in the first-line setting, as well as the potential benefits of continuing EVE+ET beyond initial progression.
Methods: Postmenopausal patients with HR+ metastatic or locally advanced unresectable BC and no prior therapy for advanced disease will receive EVE (10 mg/d) and letrozole (2.5 mg/d) until first disease progression. Upon disease progression, patients will have the option to receive EVE and EXE (25 mg/d) until further disease progression. The primary endpoint is PFS in the first-line setting. Secondary endpoints include PFS in the second-line setting, response rates, overall survival, safety, and the efficacy of oral dexamethasone solution to reduce the severity and/or duration in patients developing stomatitis.
Results: This open-label, single-arm trial will be open for enrollment in Europe, Asia, and the Americas starting in February 2013. A total of 200 patients will be enrolled. Estimated completion date is the fourth quarter of 2015.
Conclusion: This trial will provide insight into the effectiveness of EVE + letrozole in the first-line metastatic BC setting as well as the efficacy of continued EVE-based treatment following initial progression.
Disclosure of Interest: Cardoso: consultancy and research support from NVR. Bachelot: research support from NVR. Gradishar, Liedke & Azevedo: nothing. Sriuranpong: honoraria for advisory consultation from NVR, Thailand. Saletan & Graham: employees of NVR.

P272

EVEROLIMUS PLUS EXEMESTANE VERSUS EVEROLIMUS OR CAPECITABINE MONOTHERAPY IN BREAST CANCER: BOLERO-6

B. Ejlertsen[1]*, G. Jerusalem[2], S. Hurvitz[3], R. De Boer[4], T. Taran[5], T. Sahmoud[5], H. Burris[6]. *[1]Oncology, Copenhagen University Hospital, Copenhagen, Denmark, [2]CHU Sart Tilman, Liege, Belgium, [3]UCLA Medical Center, Los Angeles, United States of America, [4]Royal Melbourne Hospital, Melbourne, Australia, [5]Novartis Pharmaceuticals Corporation, East Hanover, United States of America, [6]Sarah Cannon Research Institute, Nashville, United States of America*

Goals: Everolimus (EVE), an oral inhibitor of mammalian target of rapamycin (mTOR), has clinical activity as monotherapy and in combination with endocrine therapy (Baselga, NEJM, 2012) for the treatment of hormone receptor-positive (HR+) advanced breast cancer (BC). In BOLERO-2, the addition of EVE to exemestane (EXE) more than doubled median progression-free survival (PFS) compared with EXE alone in postmenopausal women with HR+, HER2− advanced BC progressing after letrozole or anastrozole. Capecitabine, an oral 5-fluorouracil prodrug, is indicated as monotherapy for patients with locally advanced or metastatic BC after failure of taxanes and an anthracycline-containing regimen or for whom further anthracycline therapy is not indicated. Clinical activity of capecitabine monotherapy has been demonstrated in the first-line setting in patients with HR+, HER2− metastatic BC. The objective of the BOLERO-6 study is to evaluate 2 concepts of EVE in HR+, HER2− advanced BC progressing after letrozole or anastrozole: 1) PFS following EXE monotherapy compared with EVE + EXE, and 2) PFS following capecitabine monotherapy compared with EVE + EXE.
Methods: BOLERO-6 is a 3-arm, randomized, open-label, multicenter phase 2 study in which 300 patients will be randomized in a 1:1:1 ratio to receive the combination of EVE (10 mg/day) + EXE (25 mg/day) versus EVE (10 mg/day) versus capecitabine (1,250 mg/m^2 twice daily for 14 days in 3-week cycles) until disease progression or intolerable toxicity. Patients will be stratified by the presence of visceral disease. The primary endpoint is PFS for EVE + EXE versus EVE alone based on local radiologic assessment. The key secondary endpoint is PFS for EVE + EXE versus capecitabine. Additional secondary endpoints include overall survival, objective response rate, clinical benefit rate, safety, time to deterioration in Eastern Cooperative Oncology Group performance status, time to deterioration in quality of life, and patient treatment satisfaction. Efficacy assessments will be evaluated every 6 weeks.
Results: BOLERO-6 will open for enrollment in the first quarter of 2013, and estimated study completion is early 2015.
Conclusion: This study will provide efficacy and safety information on EVE + EXE versus EVE or capecitabine monotherapy in patients with HR+ HER2− advanced BC progressing after letrozole or anastrozole.
Disclosure of Interest: Ejlertsen: research support from NVR & Amgen, travel support from NVR. Jerusalem: advisor & consultant to NVR. Hurvitz: research & travel from Roche & NVR. de Boer: speaker's bureau for NVR & advisor Roche & NVR. Taran & Sahmoud: employees NVR. Burris: no disclosure.

P273

EFFECTS OF EVEROLIMUS ON DISEASE PROGRESSION IN BONE AND BONE MARKER LEVELS: OUTCOMES FROM BOLERO-2

M. Gnant[1] *, M. Piccart[2], M. Geberth[3], P. Hadji[4], M. El-Hashimy[5], S. Rao[5], T. Taran[5], T. Sahmoud[5], D. Lebwohl[5], M. Campone[6].
[1]Department of Surgery and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria, [2]Medicine, Institut Jules Bordet, Bruxelles, Belgium, [3]SPGO-Mannheim, Schwerupunktpraxis fuer Gynaekologische Onkologie, Mannheim, Germany, [4]Philipps-University of Marburg, Universitatsklinikum Giessen und Marburg, Standort Marburg, Marburg, Germany, [5]Novartis Pharmaceuticals Corporation, East Hanover, United States of America, [6]Institut de Cancérologie de l'Ouest – René Gauducheau, Centre de Recherche en Cancérologie, Nantes Saint Herblain, France

Goals: BOLERO-2, a multinational, double-blind, placebo-controlled, phase 3 study in postmenopausal women with hormone-receptor-positive advanced breast cancer (BC) progressing after nonsteroidal aromatase inhibitors (NSAIs), showed significant clinical benefits with the addition of everolimus (EVE) to exemestane (EXE) (Baselga J, et al. NEJM. 2012; 366: 520–9). Bone resorption in BC is important because it can be increased by the development of bone metastases (mets) and by the use of aromatase inhibitor therapy. In preclinical studies, mTOR inhibition was associated with decreased osteoclast survival and activity. Exploratory analyses in BOLERO-2 evaluated the effect of EVE vs placebo (PBO) on bone marker levels and BC progression in bone.

Methods: Eligible patients were treated with EXE (25 mg/d) and randomized (2:1) to EVE (10 mg/d) or PBO. Bone turnover markers were exploratory endpoints analyzed at 6 and 12 wk after treatment initiation, and included bone-specific alkaline phosphatase, amino-terminal propeptide of type I collagen, and C-terminal cross-linking telopeptide of type I collagen. Progressive disease in bone was defined as worsening of a preexisting bone lesion or development of a new bone lesion.

Results: Baseline disease characteristics, including baseline bone mets (EVE: n = 371, 76%; PBO: n = 185, 77%), were well balanced between arms (N = 724), although baseline bisphosphonate (BP) use slightly favored the control arm (44% EVE vs 55% PBO). Zoledronic acid (29% EVE vs 34% PBO) and pamidronate (6% EVE vs 7% PBO) were the most commonly used BPs at baseline. At 18-mo median follow-up, progression-free survival (primary endpoint), overall response rate, and clinical benefit rate ($P < 0.0001$, all) were significantly higher with EVE (n = 485) vs PBO (n = 239). Levels of bone turnover markers at 6 and 12 wk increased vs baseline with PBO, but decreased with EVE. The cumulative incidence rate of BC progression in bone was consistently lower for EVE vs PBO in the overall population and in patients with bone mets at baseline (n = 556). Fracture incidence was numerically lower in the EVE arm (2.3%) versus PBO (3.8%).

Conclusion: Exploratory analyses from BOLERO-2 suggest that adding EVE reduced bone turnover and BC progression in bone in patients receiving EXE therapy for BC progressing after NSAIs.

Disclosure of Interest: M. Gnant: research support from GlaxoSmithKline, Sanofi-Aventis, Novartis, Roche; consultant to Merrion, Novartis; honoraria: Amgen, Pfizer, Novartis, GlaxoSmithKline, Bayer, Sandoz, AstraZeneca, GenomicHealth.

P274

EVEROLIMUS-RELATED ADVERSE EVENTS: SAFETY INSIGHTS FROM BOLERO-2

H.S. Rugo[1] *, M. Gnant[2], M. Geberth[3], T. Csoszi[4], W. Feng[5], H. Bauly[6], M. El-Hashimy[7], T. Taran[5], T. Sahmoud[5], M. Piccart[8].
[1]Department of Medicine, University of California, San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, United States of America, [2]Department of Surgery and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria, [3]SPGO-Mannheim, Schwerupunktpraxis fuer Gynaekologische Onkologie, Mannheim, Germany, [4]Jász-Nagykun-Szolnok Megyei Hetényi Géza Kórház-Rendelointézet, Szolnok, Hungary, [5]Novartis Pharmaceuticals Corporation, East Hanover, United States of America, [6]Novartis Pharma AG, Basel, Switzerland, [7]Novartis Pharmaceuticals Corporation, Florham Park, United States of America, [8]Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium

Goals: To review the incidence and management of everolimus (EVE)-related adverse events (AEs) in patients with advanced hormone-receptor-positive (HR+) breast cancer (BC) enrolled in BOLERO-2.

Methods: Patients were randomized 2:1 to EVE 10 mg/day or placebo (PBO), in addition to open-label exemestane (EXE) 25 mg/day (N = 724). Safety evaluations included recording of AEs and dose modifications and discontinuations with EVE. Treatment was discontinued for disease progression, consent withdrawal, or unacceptable toxicity. Median follow-up duration was 18 months.

Results: The median duration of exposure to study treatment was 23.9 weeks for EVE and 29.5 weeks for EXE in the EVE+EXE arm versus 13.4 weeks for PBO and 14.1 weeks for EXE in the PBO+EXE arm. Class-effect toxicities including stomatitis, pneumonitis, infections, and hyperglycemia were mainly grade 1/2 and plateaued over time. Grade 3 class-effect toxicities occurred in <10% of patients (stomatitis [8%], pneumonitis [3%], infections [5%], and hyperglycemia [5%]). Grade 4 infections (1.5%) and hyperglycemia (0.4%) were uncommon; there were no grade 4 events of stomatitis or pneumonitis. Median time to onset for stomatitis (16 days) and hyperglycemia (29 days) was relatively short compared with that for infections (66 days) and pneumonitis (115 days); similar to phase III trials of EVE monotherapy. Treatment discontinuation of at least 1 study drug because of AEs occurred in 26% and 5% of patients in the EVE+EXE and PBO+EXE arms, respectively. More patients required dose adjustments for EVE because of AEs (62%) than for PBO (12%), and more patients had at least one dose reduction for EVE because of AEs (38%) in EVE+EXE arm than for PBO (3%) in the PBO+EXE arm. The frequency of dose modifications required for AE management of EVE was independent of patient age. Overall, the duration of dose interruptions was short and most patients resumed the full EVE dose within 2 weeks.

Conclusion: Everolimus-associated AEs were typically mild to moderate, and infrequent grade 3/4 events were adequately managed using established recommendations. Careful monitoring from initiation of therapy and timely management of EVE side effects are important to maintain patients on treatment. The AE profile in patients with advanced HR+ BC was consistent with the known EVE safety profile. Safety of EVE in the adjuvant setting will be investigated by UNIRAD.

Disclosure of Interest: HSR: Pfizer, Nov, Merck. MG: GSK, s-a, Nov, Roche, Merrion, Amgen, Pfizer, Bayer, Sandoz, AZ, Genomic Health. MP: PharmaMar, s-a, Amgen, BMS, GSK, Boehringer, Roche, Bayer, Pfizer, AZ. MG, TC: none. WF, HB, ME-H: Nov empl. TT, TS: Nov empl w/stock/opt.

P275

DIAGNOSTIC AND PROGNOSTIC ISSUES IN INFLAMMATORY BREAST CANCER

A.E. El Bastawisy*, S.S. Eisa, G. Amira, M. Hilal, R.M. Gaafar. *Medical Oncology, National Cancer Institute, Cairo University, Cairo, Egypt*

Goals: Background: Inflammatory breast cancer (IBC) has a dismal prognosis so research to differentiate IBC from other breast entities is required. Primary end points were

a. comparison of dermal lymphatic invasion (DLI) and Ki67 score in both groups.
b. comparison of clinical and pathological responses in both groups.

Secondary endpoints was the comparison of progression free survival and overall survival.

Methods: This is a prospective case control study comparing two groups of newly diagnosed patients with:

1. inflammatory breast cancer (IBC).
2. Non inflammatory locally advanced breast cancer (LABC).

In both groups: DLI, Ki 67, ER, PR, Her2neu were assessed. Neoadjuvant chemotherapy consisted of 4 cycles of FEC100 followed by modified radical mastectomy according to clinical response, postoperative chemotherapy with 2 courses of the same regimen followed by radiotherapy. Tamoxifen 20 mg po daily for 5 years in ER and or PR positive tumors starting after the completion of radiotherapy.

Results: A total of 42 patients, of them 21 cases are stage III B (T4d, N0–2 M0) IBC and 21 are stage IIIB (T4a–c,N0–2,M0) LABC, aged 28 to 68 were included and followed up from November 2007 till February 2010 with a median follow up period of 22.5 months. Toxicity of both arms, mainly hematologic, nausea and vomiting, was in general acceptable without treatment-related death. 80% of examined specimens of IBC patients showed positive DLI as compared to 16.7% of specimens of LABC patients, and the difference was statistically very highly significant (P-value ≤ 0.0001). 81.3% of IBC patients had high score Ki 67 as compared to 43.8% of LABC patients (P-value = 0.028). Objective clinical response to neoadjuvant chemotherapy in IBC arm was 57.1% (4.8% complete response, CR) as compared to 81% (9.5% CR) in LABC. (P-value = 0.09). Overall pathological response (complete pathological response, pCR +partial pathological response, pPR) was 35.3% in IBC arm compared to 40% in LABC arm, (P-value = 0.618). 1, 2 years progression free survival (PFS) were 55.87% and 37.71% respectively in IBC arm compared to 85.71%, 66.67% in LABC, (P-value = 0.072). 1 and 2 years overall survival (OS) were 69.82% and 51.20% respectively in IBC arm compared to 95.24%, 95.24% in LABC arm (P-value = 0.0038).

Conclusion: Positive DLI and High score Ki 67 are valid diagnostic tools for IBC. IBC should be considered as a separate entity.

Disclosure of Interest: No significant relationships.

P276

BOLERO-2: EFFICACY AND SAFETY OF FIRST-LINE EVEROLIMUS PLUS EXEMESTANE IN ADVANCED BREAST CANCER

M. Campone[1]*, M. Gnant[2], P. Neven[3], B. Pistilli[4], H.S. Rugo[5], J. Baselga[6], H. Bauly[7], T. Taran[8], T. Sahmoud[8], G. Hortobagyi[9]. *[1]Centre de Recherche en Cancérologie, Institut de Cancérologie de l'Ouest – René Gauducheau, Centre de Recherche en Cancérologie, Nantes Saint Herblain, France, [2]Medical University of Vienna, Medical University of Vienna, Vienna, Austria, [3]University Hospitals Leuven, Leuven, Belgium, [4]Presidio Ospedaliero di Macerata-Zona Territoriale, Macerata, Italy, [5]Department of Medicine, University of California, San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, United States of America, [6]Memorial Sloan Kettering, New York, United States of America, [7]Novartis Pharma AG, Basel, Switzerland, [8]Novartis Pharmaceuticals Corporation, East Hanover, United States of America, [9]The University of Texas MD Anderson Cancer Center, Houston, United States of America*

Goals: In the BOLERO-2 study, progression-free survival (PFS) was significantly longer with the combination of everolimus and exemestane (EVE+EXE) compared with placebo (PBO) and EXE (hazard ratio=0.45; P < 0.0001). Consistent efficacy results were observed in all subgroup analyses, such as in patients with visceral metastases, patients who recurred after adjuvant endocrine therapy alone, or in patients who recurred after adjuvant endocrine therapy plus chemotherapy. This analysis of BOLERO-2 examines the efficacy of EVE+EXE in the subgroup of patients who received treatment after adjuvant therapy (ie, as first-line therapy in the advanced setting).

Methods: BOLERO-2 enrolled patients with hormone-receptor-positive (HR+) advanced breast cancer who had a recurrence or progressed after prior nonsteroidal aromatase inhibitors, and compared EVE (10 mg/d) + EXE (25 mg/d) versus PBO+EXE. The primary endpoint was PFS by local investigator review.

Results: A total of 137 patients received first-line EVE+EXE (n = 100) or PBO+EXE (n = 37) in the advanced setting. Of these patients, 74% of the EVE+EXE arm and 76% of the PBO+EXE arm had progressed after adjuvant endocrine therapy plus chemotherapy; 26% and 24%, respectively, had progressed after adjuvant endocrine therapy alone. The EVE+EXE group had significantly longer PFS compared with the PBO+EXE group (11.50 vs 4.07 mo, respectively; hazard ratio=0.39; 95% confidence interval, 0.25–0.62). Median PFS remained longer with EVE+EXE versus PBO+EXE regardless of whether chemotherapy was included with the prior adjuvant hormonal therapy. Similar results were obtained from the analyses based on central review. The safety profile was consistent with the known profiles of each agent.

Conclusion: EVE+EXE prolonged PFS in patients with HR+ advanced breast cancer who received treatment as first-line therapy. These results support the combination of EVE+EXE in patients progressing after adjuvant therapy. The recently initiated BOLERO-4 study is also evaluating the efficacy of EVE as a first-line therapy in patients with HR+ advanced breast cancer.

Disclosure of Interest: MC: Nov. MG: GSK, s-a, Nov, Roche, Merrion, Amg, Pfiz, Bay, Sandoz, AZ, GenHlth. HSR: Pfiz, Nov, Merck. JB: Nov, Roche, Merck, s-a, Verastem, Bay, Chugai, Exelixis, Onyx, Constell. TS, TT: Nov emp w/stock. HB: Nov emp. GNH: Allergan, Nov, Gntech, s-a.

Health politics/Guidelines

P280
COMPLIANCE WITH THE NCCN GUIDELINES IN THE STAGING OF BREAST CANCER PATIENTS

S. Alfotih[1] *, T.M. Alqurashi[2], M. Alsayegh[2], N. Birido[3]. [1]*Medical Oncology, King Fahad Specialist Hospital – Dammam, Dammam, Saudi Arabia,* [2]*King Fahad Specialist Hospital – Dammam, Dammam, Saudi Arabia,* [3]*Surgery, King Fahad Specialist Hospital –Dammam, Dammam, Saudi Arabia*

Goals: King Fahad Specialist Hospital – Dammam (KFSH-D) is a tertiary centre in the Eastern Region of Saudi Arabia. New breast cancer referrals are evaluated at a Multidisciplinary Breast Clinic (MDBC). Staging investigations are requested along the National Comprehensive Cancer Network (NCCN) guidelines. Our objective is to assess compliance with staging guidelines and the consequences of deviating from the recommended investigations.
Methods: A retrospective review of the medical records of patients who attended the MDBC from January 2011 to December 2012 was performed. Patients with pathology not confirming cancer or deficient information were excluded. Compliance was assessed by comparing investigations with the recommendations of the NCCN guidelines for each clinical stage.
Results: A total of 355 medical records were reviewed. Thirty-three patients were excluded. From the remaining 322 patients, 129 (40%) were stage III and IV, and 193 (60%) were stage 0–II according to the American Joint Commission on Cancer Classification. Our practice showed compliance with the NCCN guidelines in 202 patients (63%). In 120 (37%) patients guidelines were not followed. Of the latter group only five had advanced stage (under investigated) and 115 (96%) were stage 0–II. These represented 60% of the total patients diagnosed with early breast cancer (stage 0–II). These non indicated staging investigations generated further investigations like MRI, PET or follow up CT in 24 (21%). Seven patients (3.6%) of those who were over investigated (presumed stage 0–II) were found to have distant metastasis. In comparison, 43 (33.3%) of those with advanced stage had investigations suggestive of metastatic disease.
Conclusion: This study showed a tendency to over investigate patients with early breast cancer and an overall compliance of 63% with the NCCN guidelines in the staging of breast cancer. Staging investigations in early breast cancer have an impact on cost; causes delay in patient management and may increase their anxiety, particularly when further investigations are generated. Application of care pathways that incorporate guidelines should be established to prevent deviation from recommendations.
Disclosure of Interest: No significant relationships.

P281
RETROSPECTIVE BUDGET IMPACT ANALYSIS ON THE USE OF THE ONCOTYPE DX® TEST IN IRELAND

M. Falahee[1] *, J. Plun-Favreau[2], K. Ercoli[2]. [1]*International, Genomic Health, Co. Cork, Ireland,* [2]*Reimbursement & Market Access, Genomic Health International Sàrl, Geneva, Switzerland*

Goals: Oncotype DX® is a genomic test providing information on the likely benefit of adjuvant chemotherapy in patients with early stage, ER+, HER2-, N0 breast cancer. Ireland was the first country in Europe to publicly reimburse the Oncotype DX® test in October 2011. This study aimed at analysing the real life budget impact associated with the use of the Oncotype DX® test in the Irish clinical practice from the perspective of the Health Service Executive (HSE).
Methods: A model was developed to assess the impact on treatment decisions and cost to the HSE associated with the use of the Oncotype DX® test in the Irish clinical practice. The Oncotype DX® test results (i.e. Recurrence Score) for patients covered through HSE were collected retrospectively for each hospital (Cork University hospital, St Vincents', St James, Midwestern, Mater, Beaumont, Galway and Waterford) from the Genomic Health commercial database. All publicly insured patients were referred to these hospitals and treatment decisions were discussed in multi-disciplinary teams. Clinical decisions before and after the availability of the Oncotype DX® test results were collected through a survey of clinical practice among physicians practicing in each hospital. Chemotherapy cost data including chemotherapy drugs, administration, monitoring and adverse events was collected from the hospitals and from the Casemix database.
Results: Physicians consistently indicated that they were using the test in patients who were candidates for chemotherapy in order to save un-necessary treatments. Physicians reported consistent decision making following low scores (no chemotherapy) and high scores (chemotherapy). However, clinical practice differed in the group of patients with intermediate scores. Between 1st of October 2011 and 29th of September 2012, 342 Oncotype DX® tests were ordered for patients covered through the HSE. Among those, 256 (75%) patients were not given adjuvant chemotherapy. Taking into account the public price of the Oncotype DX® test, it is estimated that € 856,440 were saved by the HSE. Unlike cost-effectiveness analyses, this budget impact analysis only takes into account the short term cost of chemotherapy. It is providing important information on how the test was used and what impact it had on the HSE budget.
Conclusion: Since it got reimbursed in Ireland in October 2011, the Oncotype DX® test allowed the HSE to save a significant chemotherapy budget.
Disclosure of Interest: Mike Falahee is an employee of Genomic Health Int.

P282
COST SAVINGS WITH HERCEPTIN® (TRASTUZUMAB) SC VS IV ADMINISTRATION: A TIME & MOTION STUDY

S. Nawaz[1] *, K. Samanta[2], S. Lord[3], V. Diment[4], S. Mcnamara[2]. [1]*Medical Affairs, Roche Products Limited, Welwyn Garden City, United Kingdom,* [2]*Health Economics and Strategic Prcing, Roche Products Limited, Welwyn Garden City, United Kingdom,* [3]*Marketing, Roche Products Limited, Welwyn Garden City, United Kingdom,* [4]*Clinical Projects Group, Roche Products Limited, Welwyn Garden City, United Kingdom*

Goals: To quantify active health care professional (HCP) time (i.e. nurse, pharmacist, technician and assistant hours) and costs associated with the administration of Herceptin subcutaneous (SC) injection [via single-use injection device (SID)] and Herceptin intravenous (IV) infusion in the treatment of patients with HER2-positive early breast cancer within the PrefHer trial setting; secondly, to describe patient time in the care unit and patient infusion chair time for both routes of administration (RoA).
Methods: A UK multi-centre prospective, observational Time & Motion study was run alongside the PrefHer trial (ClinicalTrials.gov id: NCT01401166). Trained observers monitored the duration of each Herceptin SC and IV related task that HCPs were actively engaged in, and separately patient time in the care unit and infusion chair time, and recorded the times on paper Case Report Forms. Type and quantity of medical consumables used with each RoA were also collected. In total, 24 Herceptin patient episodes were recorded (12 SC, 12 IV). Mean total administration time was calculated as the mean sum of task times, for both IV and SC. The mean cost of each RoA was calculated as the mean cost of HCP time plus the mean cost of consumables used. HCP time was costed using Personal Social Services Research Unit and National Health Service banded salaries. Consumables were costed using hospital pharmacy data and online sources.
Results: Mean active HCP time for IV administration was 92.6 minutes. Mean active HCP time for SC administration was 16

minutes. Mean cost for IV administration was £144.96 (£132.05 of HCP time and £12.92 of consumables). Mean cost for SC administration was £33.03 (£32.39 of HCP time and £0.64 of consumables). This suggests that SC administration of Herceptin could lead to a time saving of 76.6 minutes versus IV, or a total cost saving of £111.93 per patient episode. This equates to a potential saving of £2014.74 over a full course of treatment (18 cycles). Mean time spent in the care unit and in the infusion chair were 94.5 minutes and 75 minutes respectively for IV, and 56.7 minutes and 30 minutes respectively for SC.

Conclusion: Conversion from IV to SC Herceptin may lead to a substantial reduction in active HCP time, consumables used and overall costs. Consequently, any savings generated could be reinvested elsewhere in order to improve overall patient care.

Disclosure of Interest: Authors work for Roche Products Limited

P283

COST-EFFECTIVENESS ANALYSIS OF THE 21-GENE BREAST CANCER TEST IN MEXICO

J. Bargallo Rocha[1]*, F. Lara Medina[1], R. Shaw Dulin[1], V. Pérez Sánchez[1], C. Villarreal Garza[1], H. Maldonado Martínez[1], A. Mohar Betancourt[1], W. Valentine[2]. *[1]Breast Cancer Department, Instituto Nacional de Cancerólogа, Ciudad de México, Mexico, [2]Ossian communications, Basel, Switzerland*

Goals: The Oncotype DX® Breast Cancer Test is a validated 21-gene assay that predicts the likely benefit from adjuvant chemotherapy in patients with early-stage, N0–3, ER+ breast cancer. This test was shown to be cost-effective versus clinical practice in several countries however none of these studies were conducted in Mexico. The aim of this analysis was to evaluate the cost-effectiveness of using the Oncotype DX® test to inform adjuvant chemotherapy decisions in Mexico.

Methods: A Markov model was developed to make long-term projections of distant recurrence, survival, and direct costs for the eligible patients. Scenarios using standard care or Oncotype DX® to inform treatment recommendations for adjuvant chemotherapy were modeled based on a recent meta-analysis of studies investigating the decision impact of Oncotype DX®. Transition probabilities and risk adjustment were based on published landmark trials. Costs (2011 Mexican Pesos [MXN]) were estimated from the Instituto Mexicano del Seguro Social (IMSS) perspective based on published data identified by literature review. In line with Mexican pharmacoeconomic guidelines, future costs and clinical benefits were discounted at 5% annually. Sensitivity analyses were performed.

Results: Following Oncotype DX® testing, 29.5% of early-stage breast cancer patients were spared chemotherapy whilst 5.6% of patients received chemotherapy in addition to hormone therapy. Long-term modeling analysis showed that optimized therapy allocation following Oncotype DX® testing led to an improvement in mean life-expectancy of 0.068 years per patient and increased direct costs by MXN 1,707 per patient versus usual care. This equated to an incremental cost effectiveness ratio (ICER) of MXN 25,244 (US$ 1,960) per life-year gained, well below the accepted cost-effectiveness threshold that equals the GDP per capita (i.e. MXN 142,843). In a secondary analysis of patients previously recommended chemotherapy, use of Oncotype DX® was associated with avoidance of chemotherapy in 46% of patients, leading to cost savings of MXN 27,414 (US$ 2,129) per patient, with life expectancy maintained at the level expected with standard care.

Conclusion: Using the Oncotype DX® breast cancer test in the Mexican clinical practice is expected to be cost-effective in the whole eligible population and cost-saving if used selectively in patients that would be recommended chemotherapy in standard care.

Disclosure of Interest: No significant relationships.

P284

COST-EFFECTIVENESS OF ONCOTYPE DX® TEST VS CURRENT CLINICAL PRACTICE: A DUTCH COST PERSPECTIVE

R. De Jonge[1]*, L. Steuten[2], M. Schutten[3], M. Kip[3], H. Monteban[1]. *[1]Market Access, Monteban Value Services, Amerongen, Netherlands, [2]Panaxea BV, University of Twente, Enschede, Netherlands, [3]Health Economics and Reimbursement, Panaxea BV, Enschede, Netherlands*

Goals: The aim of this study was to evaluate the expected incremental cost-effectiveness of Oncotype DX® testing to support adjuvant therapy decision making vs. current clinical practice in the treatment of patients with ER+, early-stage breast cancer in the Netherlands.

Methods: A Markov model was developed to project distant recurrences, survival, quality-adjusted life years (QALYs) and direct medical costs for patients with ER+, node-negative or micrometastatic (pN1mic) early-stage breast cancer, over a time horizon of 30 years from a Dutch health systems perspective. The model compared Oncotype DX® testing to inform treatment recommendations to conventional diagnostic procedures including Adjuvant! Online. The model was run with NL-specific life tables for mortality and 3 respective datasets for net change in treatment recommendations following Oncotype DX® testing. A published meta-analysis (Hornberger et al. 2011) on treatment recommendations with and without Oncotype DX® served as the base case for the model; alternative model runs were based on a landmark Oncotype DX® study in Germany (Eiermann et al. 2012) and one in Wales (Holt et al. 2011). Costs (in 2012 euros) were derived from published NL sources. Following Dutch pharmacoeconomic guidelines, future costs were discounted at 4% and clinical benefits at 1.5% annually. A probabilistic sensitivity analysis was performed.

Results: Oncotype DX® was projected to increase mean expected life years (LY) by 0.07 to 0.23 years and mean expected QALYs by 0.20 to 0.36. Clinical benefits were driven by optimized allocation of adjuvant chemotherapy in the Oncotype DX® group. Depending on which dataset was used, direct medical costs were estimated to be lower or slightly higher with Oncotype DX® testing. This led to a range of incremental cost-effectiveness ratios (ICERs) from cost-saving to €626/LY and €717/QALY gained. Cost-effectiveness of Oncotype DX® testing was sensitive to net changes in chemotherapy for low risk patients.

Conclusion: Reallocation of adjuvant chemotherapy based on Oncotype DX® test results was associated with improvements in long-term survival and QALYs in this modeling analysis. The ICERs indicated that Oncotype DX® would be cost saving or highly cost-effective. At a willingness to pay threshold of €20,000/QALY (lowest cost-effectiveness threshold applied in NL), probabilistic sensitivity analysis showed a 100% probability that Oncotype DX® testing would be cost-effective versus current clinical practice in the Netherlands.

Disclosure of Interest: This study was financially supported by an unrestricted grant from Genomic Health. The views presented are solely the authors'.

P285

COST-EFFECTIVENESS OF EVEROLIMUS FOR ENDOCRINE RESISTANT HR+ METASTATIC BREAST CANCER

M. Liu[1]*, K. Matter-Walstra[1], T.D. Szucs[1], K.J. Dedes[2]. *[1]Institute of Pharmaceutical Medicine/ecpm, University of Basel, Basel, Switzerland, [2]Department for Gynecology, University Hospital of Zurich, Zürich, Switzerland*

Goals: The addition of Everolimus to Exemestane significantly prolongs progression free survival for women with hormone receptor positive metastatic breast cancer resistant to aromatase inhibitors. We sought to evaluate the cost-effectiveness of this new regimen.

Methods: A Markov cohort simulation based on the randomized controlled trial BOLERO-2 was used to follow the clinical course of patients. Input parameters were based on the clinical data presented

in the trial, while direct costs, reported in Euros (2012), were assessed from the perspective of the Swiss health system.

Results: In the base case scenario, the addition of everolimus to exemestane is estimated to cost an additional 25'129€ and to yield a gain of 0.32 quality-adjusted life years (QALYs), resulting in an incremental cost-effectiveness ratio of 77'997€ per QALY gained. The ICER was most sensitive to progression-free survival in the combination arm, post-progression survival in both arms and the utility value for stable disease, while being almost completely inelastic to treatment times for exemestane in both arms as well as the variables related to adverse events. Probabilistic sensitivity analysis showed that the generally accepted threshold value of 83'000€ (or 100'000 Swiss Francs) was met in 52.9% of the samples. Because post-progression survival was poorer in the combination treatment arm despite better overall survival, possibly caused by a confounding effect, an alternative model was considered to eliminate this by assuming identical post-progression survival, yielding an ICER of 50'230€ per QALY, with 83.6% of the cases meeting the willingness-to-pay threshold in the probabilistic sensitivity analysis.

Conclusion: Although the combination treatment with everolimus showed a tendency to be cost-effective in the primary model, the projected outcomes were too close to the willingness-to-pay threshhold to render a conclusive judgement. Depending on the clinical relevance of the potential confounding effect, the addition of everolimus could be more cost-effective than is suggested by the base case scenario. Further investigation is however required.

Disclosure of Interest: No significant relationships.

P286
ECONOMIC IMPACT OF ONCOTYPE DX® RESULTS GUIDED ADJUVANT TREATMENTS IN HUNGARY

K. Boér[1]*, P. Rózsa[2], Z. Horváth[3], É. Juhos[4], G. Rubovszky[4], Z. Kahán[5], Z. Lőcsei[6], Zsuzsanna Nagy[7], Z. Pápai[8], Zoltán Nagy[9]. *[1]Oncology Departement, Szent Margit Hospital, Budapest, Hungary, [2]MediConcept Ltd., Budapest, Hungary, [3]University of Debrecen, Debrecen, Hungary, [4]National Institute of Oncology, Budapest, Hungary, [5]University of Szeged, Szeged, Hungary, [6]University of Pécs, Pécs, Hungary, [7]Szent Imre Hospital, Budapest, Hungary, [8]Hospital of Hungarian Army, Budapest, Hungary, [9]Med Gen-Sol Ltd., Budapest, Hungary*

Goals: Role of hormonal therapy (HT) is well established in node negative (N0) estrogen-receptor positive (ER+) early breast cancer (EBC). However benefit of chemotherapy (CT) in patients with N0, ER+ EBC would be small. Oncotype DX® (ODX) provides additional predictive and prognostic information beyond traditional clinical and pathological markers. International guidelines support use of Oncotype DX® test to evaluate risk of recurrence and predict the benefit of CT in ER+ EBC. Our goal is to examine and show health economic value and budget impact of ODX in a small group of patients (15 patients) with ER+ EBC with chemotherapy recommendation of the Tumor board – based on traditional clinical and pathological criteria.

Methods: Fifteen ODX tests were performed in selected HR+ EBC patients. Eligibility criteria for testing were: T1c, T2, N0, N1mi, ER+ (min. 50%) and HER-2 negative EBC. In addition 2 of the following criteria were allowed: Grade III histology, Ki67 >15%, LVI+, age <40 y. Patients with clear treatment preferences were excluded. Information about adjuvant treatment plan was collected before and after obtaining ODX Recurrence Score. There was an agreement that in case of a Recurrence Score (RS) lower than 25 – HT will be the choice of therapy. In cases when RS is equal to, or higher than 25 both CT+HT therapy will be administered (considering patient's preference in intermediate group). We registered treatment decisions before and after ODX tests. We calculated and compared total costs of registered treatments and side-effects without ODX and total costs of the treatments following ODX testing.

Results: Among women with EBC use of the ODX test changed treatment recommendations (from HT+CT to HT alone) in 64% of cases (9/14). Reimbursement criteria were not allowed use test for all eligible patients, but only patients with a doubt about the value of chemotherapy. We found 1 patient Her2+ by both ODX RT-PCR and IHC testing and was excluded from final evaluation. Based on preliminary data we found ICER = −0.7 kEURO/QALY (these are intermediary results and final results will be presented in the poster).

Conclusion: We found ODX cost saving technology in selected ER+, EBC patients in Hungary. Final details, patients' characteristics and suggested treatments will be presented in frame of the poster.

Disclosure of Interest: Zoltan Nagy has commercial relationship with Genomic Health Inc.

P287
USING THE RECURRENCE SCORE IN CLINICAL PRACTICE: AN HMO EXPERIENCE WITH A UNIFIED TESTING POLICY

N. Siegelmann-Danieli[1]*, B. Silverman[2], A. Zick[3], A. Beit-Or[2], G. Hodik[2], I. Katzir[2], A. Porath[2]. *[1]Oncology Service Line, Maccabi Healthcare Services, Tel Aviv, Israel, [2]Maccabi Healthcare Services, Tel Aviv, Israel, [3]Hadassah Medical Center, Jerusalem, Israel*

Goals: This work summarizes the experience of Maccabi Healthcare Services (MHS; the 2nd largest HMO in Israel) with Oncotype DX® (ODX) testing in early breast cancer and the association of the Recurrence Score (RS; the ODX result) with treatment decisions and clinical outcomes.

Methods: The MHS eligibility criteria for ODX testing are: ER+ N0/pN1mic tumors, discussion of test implications with an oncologist, ductal carcinoma 0.6–1.0 cm with grade 2–3 histology, or HER2− ductal carcinoma 1.1–4.0 cm with grade 1–2 histology, or lobular carcinoma. Large (≥1.0 cm) grade 3 tumors could have grade reassessed. We linked up RS results to information on pts' demographics, treatments, and clinical outcomes extracted from the MHS database. Chi-squared test/Fisher exact test were used to study the association between RS, clinicopathologic characteristics, and treatments received.

Results: In the 1/2008–12/2011 timeframe, 751 MHS pts underwent ODX testing, of whom 713 met the MHS criteria; 59%, 33% and 8% of pts had low, intermediate, and high RS, respectively. RS distribution varied significantly by age ($P = 0.0458$); high RS was more common in younger than older pts (13% vs 6% in pts aged 18–44 and ≥65 yrs, respectively). In MHS-eligible pts, RS distribution varied by histology and grade. High RS was more common in IDC than ILC/mixed histology (8% vs 2%; $P = 0.0187$ for comparing RS distributions). When reviewing IDC tumors by grade and size (per the MHS policy), high RS was common even in small (≤1 cm) grade 3 tumors and was rare in large (1.1–4.0 cm) grade 1 tumors (32% vs 3%; $P < 0.0001$). Analysis of the 392 pts that had Ki-67 data revealed a weak ($r = 0.32$) positive correlation between Ki-67 levels and RS results ($P < 0.0001$). Chemotherapy was administered to 2%, 18%, and 66% of pts with low, intermediate, and high RS, respectively ($P < 0.0001$). For intermediate RS pts, older age was significantly associated with decreased chemotherapy use (47%, 14%, and 5% of pts aged 18–44, 45–64, and ≥65 yrs received chemotherapy, respectively; $P < 0.0001$). With a median follow up of 26 months, no systemic recurrences were documented; 1 pt had local recurrence.

Conclusion: Our results demonstrate that even in this seemingly low-risk population, a considerable proportion of pts (41%) had intermediate/high RS. In patients with intermediate RS, older age was significantly associated with decreased chemotherapy use.

Disclosure of Interest: No significant relationships.

Supportive care/Psychology

P288
Abstract withdrawn

P289
THE PERCEPTIONS OF ISRAELI WOMEN WITH BREAST CANCER OF THE BREAST CANCER NURSE

I. Kadmon*. *School of Nursing, Hadassah Medical Association, Jerusalem, Israel*

Introduction: The role of the Breast Care Nurse Specialist (BCN) has been developing in the last decades in some Western countries, mainly the UK, Australia, US and Israel. This newly recognized position encompasses within it the involvement of nurses as patient advocates, looking at issues such as breaking bad news and receiving the diagnosis, the participation of women in the decision-making regarding their care and navigating the women within the complex and ever demanding health care system. In this new paradigm of care, it is the woman and her significant others who are in the center, and the role of the Breast Care Nurse Specialist is of a counselor, information provider and supporter, who makes sure the woman understands the complex and sophisticated options of care. The purpose of this research is, therefore, to examine the impact that Breast Care Nurses have on Israeli women who are diagnosed with breast cancer.
Patients and Methods: About 300 women with non-metastatic breast cancer (At seven institutions) were given two questionnaires: a demographic questionnaire developed for this study, and the Ipswitch Patient Questionnaire, comprised of 21 questions, each divided to sub-questions. The questionnaire is focused on the following aspects of nurse's care: information about the role, coordination of care, provision of information, psychological and mental support, practical support and referral to other health care professionals.
Results: The stay results emphasised the general positive attittue and perceptions that women had towards all aspects of the role of the BCN as were assessed. Detailed results and descriptions of the women's views as analysed will be further presented.
Conclusions: This study was an attempt to provide a national multi-centric study evaluating the role of the BCNs in Israel. This complex, demanding and multidimensional role has been examined and evaluated in various relevant domains. These results emphasized the importance of the role and its contribution to women with breast cancer and their dear ones. Furthe rstudies need to look at the impact of the role on the health care system and and other colleagues and also at different cultures.
Disclosure of Interest: No significant relationships.

P290
FAMILY LIFE DURING AND AFTER BREAST CANCER TREATMENT: A EUROPEAN PATIENT SURVEY

D. Zarca[1]*, S. Mimoun[2], D. Elia[3], J. Braybrooke[4], B. Pinder[5], A. Lloyd[5], K. Breheny[5], M. Lomazzi[6], B. Borisch[6]. *[1]Service De Chirurgie, Clinique du Trocadéro, Paris, France, [2]Personal Practice, Paris, France, [3]Personal Practice, Paris, France, [4]Bristol Haematology and Oncology Center, Bristol, United Kingdom, [5]Oxford Outcomes, London, United Kingdom, [6]Institut De Médecine Sociale Et Préventive, Université de Genève, Geneva, Switzerland*

Goals: Family and friends play an important role for patients with breast cancer but the support they provide and the impact that breast cancer treatment may have on family life is not well documented. The aim of this pilot study was to describe breast cancer patients' experience of family life during and after chemotherapy treatment.
Methods: 192 women, aged between 18 and 65, who had received chemotherapy treatment for early stage, hormone receptor positive breast cancer, completed an online survey. The survey was conducted in 3 countries: UK (33%), France (39%) and Germany (28%). Recruitment was mainly conducted via patient organisations. The survey was developed following a literature review of existing instruments and input from several expert panels.
Results: On average, participants completed chemotherapy 31.9 months ago (SD 13.6). Overall 140 participants (70%) had children, 97 of them (49%) had children requiring being looked after. From this subgroup, 59 participants (61%) required help to take care of their children during chemotherapy. The majority (above 70%) received support from their partners and/or family members/relatives, whereas a minority required paid help (27%). Overall 113 participants (57%) required support for looking after themselves, mainly provided by their partners. Help was needed for household chores and transportation to attend medical appointment. The younger age groups (18–44 years) required more support (71%) compared to the older age groups (45–65 years) (53%). A greater number of participants in France (41%) reported receiving help from their relatives, in comparison with participants in the UK (26%) and Germany (27%). 20% of the participants required assistance for self-care, mainly in France and in the UK. No participants in the UK reported receiving paid help, in comparison to 32% in France and 20% in Germany. Nearly a third of the participants (30%) reported being unable to perform their former family role; however 63% reported being happy with the emotional support received from their family. Above 50% reported being closer to their family after completing chemotherapy.
Conclusion: These findings suggest that families actively support patients with their daily activities during treatment for early breast cancer. Additional research should be conducted to further explore the impact on and the role of the family in breast cancer.
Disclosure of Interest: Dr Zarca is an advisory board member for Genomic Health

P291
THE FACTORS AFFECTING UPTAKE OF GENETIC TESTING IN HIGH-RISK PATIENTS

Y. Sun*, E. Kang, D. Kim, E.J. Hwang, Y. Hwang, C.K. Yom, S.W. Kim. *Surgery, Seoul National University Bundang Hospital, Seongnam, South Korea*

Goals: Individuals at risk of hereditary breast and ovarian cancer face the decision whether to obtain BRCA genetic testing. The purposes of our study are to determine the rate of obtaining genetic testing and reasons of non-uptake, and to identify the factors affecting uptake of BRCA genetic testing.
Methods: We identified 804 individuals who had genetic counseling for BRCA mutation in Seoul National University Bundang Hospital from July 2003 to September 2012. The genetic counseling was performed for the 652 index cases with breast cancer and 152 family members of probands with BRCA mutation.
Results: Out of all of the index cases, 574 (88%) patients decided to be tested for BRCA mutation after the genetic counseling. The mean age of persons who had the genetic testing was younger than that of persons who did not (43.2 vs. 45.8 years old, $p = 0.058$). The rate of uptake of the genetic testing in male (91.7%) was not statistically different compared to that in female (87.9%, $p = 1.000$). In multivariate analysis, a family history of breast cancer was shown to be an independent variable affecting uptake of the genetic testing (OR 3.032; 95% CI 1.136–8.090). Among 136 persons who did not uptake genetic testing initially, 67 (47%) postponed the decision, 35 (25%) needed time to discuss with family members and 21 (15%) did not want to know whether they had BRCA mutation or not. 19 (13%) refused the test because of financial problems. Prior to national health insurance cover, 57.9% of patients did not undertake the testing due to cost. However, after the insurance coverage, non-uptake rate due to cost presented to be 6.8%, which is relatively low.

Finally, more than 40% of initial non-uptake persons had genetic testing.

Conclusion: In our institution, the rate of obtaining BRCA genetic testing was comparatively high. The family history of breast cancer was the important factor associated with uptake of the genetic testing. During the genetic counseling, we have to understand these issues and consider several factors that may influence the individual's decision.

Disclosure of Interest: No significant relationships.

P292

SEDENTARY LIFESTYLE AND PHYSICAL ACTIVITY LEVELS IN PATIENTS RECEIVING ADJUVANT CHEMOTHERAPY

A. Tonosaki[1]*, M. Ishikawa[2]. [1]*Oncology Nursing, National College of Nursing, Japan, Kiyose, Tokyo, Japan,* [2]*National Cancer Center Hospital East, Kashiwa, Chiba, Japan*

Goals: We evaluated the metabolic equivalent (MET) and physical activity level (PAL) in Japanese subjects receiving adjuvant chemotherapy.

Methods: Subjects who consented to participate in this study were patients at an outpatient clinic aged 20–64 with stage I–IIIA initial breast cancer whose regimen included anthracycline. Subjects wore a triaxial accelerometer (Panasonic Electric Works Co., Ltd., Osaka, Japan) on a waist belt, and their physical activity levels were measured for a 14-day period beginning on day 1 of chemotherapy. The Cancer Fatigue Scale was administered on days 7 and 21 (the first day of the next chemotherapy cycle). The accelerometer was used to calculate the number of steps, PAL, and total minutes spent during activities of <1.5 Mets, 1.5–2.9 Mets, and ≥3.0 Mets during the first half (FH; days 2–7) and second half (SH; days 8–14) of the study. PAL was expressed as total daily energy expenditure divided by daily basal metabolic rate, with a mean value of 1.6 (Ministry of Health, Labour and Welfare, Japan). Pearson's correlation coefficient and multiple regression analysis were used to investigate the correlation between PAL, total minutes of Mets intensity levels and fatigue scores.

Results: The mean age of the 28 subjects was 49.5 years. During FH, the mean number of steps was 3841.1 steps/day and mean PAL was 1.43; during SH, the mean number of steps was 4058.4 steps/day, mean PAL was 1.43, and mean activity times at each level per day were 195.1 min at <1.5 Mets, 313.4 min at 1.5–2.9 Mets, and 21.9 min at ≥3 Mets. Mean fatigue score during FH was 21.8, above the level causing impairment of activities of daily living, but this decreased significantly to 16.8 (normal) in SH ($p < 0.013$). Multiple regression analysis of factors that exhibited significant correlations as independent variables and PAL during SH as the dependent variable showed that PAL during SH was significantly associated with mean time spent during activities of 1.5–2.9 Mets ($\beta = 0.880$, $p = 0.000$) and 3.0 Mets ($\beta = 0.268$, $p = 0.000$).

Conclusion: Patients receiving adjuvant chemotherapy have extremely low PAL, and can be regarded as having a sedentary lifestyle. PAL in these patients did not recover by the start of the next cycle of chemotherapy, and if this condition is prolonged, they may be at high risk of developing metabolic and cardiovascular complications.

Disclosure of Interest: No significant relationships.

P293

PSYCHOSOCIAL INTERVENTION PROGRAM FOR YOUNGER WOMEN WITH EARLY BREAST CANCER

P. Heras*, V. Niarou. *Internal Medicine, General Hospital of Nafplio, Athens, Greece*

Goals: It has been shown that younger women with early breast cancer may experience greater psychosocial distress than older women with early breast cancer. This is commonly attributed to differences in stage-of-life issues (e.g., desiring a romantic relationship or being in the early stages of one, desire for children or parenting children, career) as well as severity of disease. Here we: (1) provide pilot data on the psychometric properties of a screening instrument to discern distress in younger women with early breast cancer; and, (2) report the results of a pilot study of an eight-week group-based psychosocial intervention tailored to the needs of younger women with early breast cancewr.

Methods: 37 women with early breast cancer who were 45 years of age and younger (mean = 36) were recruited to participate. Women who were enrolled participated in a one-hour individual assessment followed by 8 one-and-a half hour group sessions. The following assessment battery was conducted at baseline ('pre'), after completion of the 8 group sessions ('post'), and 2 months later ('2mo'): Functional Assessment of Cancer Therapy-Breast (FACT-B), Center for Epidemiologic Studies-Depression Scale (CESD), Menopausal Rating Scale (MRS). Data were analyzed using repeated measures analysis of variance.

Results: Participants showed a significant reduction in CESD scores (Pre = 18.09 ± 4.56, Post = 11.36 ± 2.78, 2mo = 12.09 ± 3.07, $p = 0.018$) and FACT-B Functional Well Being Subscale scores (Pre = 14.67 ± 1.44, Post = 17.73 ± 1.45, 2mo = 18.00 ± 1.76, $p = 0.046$). Total scores on the MRS and the FACT-B did not show a significant change. Data on the psychometric properties of the Young Breast Vancer Distress Screening Instrument will also be presented.

Conclusion: Young early breast cancer patients have unique psychosocial needs compared to their older counterparts. A time-limited group intervention that offers a tailored program of education, coping skills, support and emotional processing is an effective way to reduce depression and increase quality of life in young early breast cancer patients.

Disclosure of Interest: No significant relationships.

P294

URINARY INCONTINENCE AND ITS IMPACT ON QUALITY OF LIFE IN EARLY BREAST CANCER

P. Heras*, V. Niarou. *Internal Medicine, General Hospital of Nafplio, Athens, Greece*

Goals: The prevalence and severity of menopausal symptoms such as hot flashes and their impact on quality of life in early breast cancer (BC) survivors are well-documented. Considerably less is known about urinary incontinence (UI), a genitourinary symptom commonly associated with menopause. The pusrpose of thiw pilot study was to examine the prevalence of UI symptoms in early BC survivors and the relationship of UI severity to survivors' quality of life.

Methods: A convenience sample of 45 early BC survivors treated with chemotherapy competed the Incontinence Severity Index (ISI), the Urogenital Distress Inventory Short Form (UDI-6) and the Incontinence Impact on Life Questionnaire-Short Form (IIQ-7).

Results: Mean age of participants was 58.7 years (SD = 9.3). Sixty-nine percent were postmenopausal before treatment and 87% were postmenopausal following treatment. Sixty-seven percent of survivors reported symptoms associated with UI, including frequent urination (43%), urine leakage related to urgency (47%) and leakage related to physical activity, coughing or sneezing (53%). Thirty-eight percent reported leakage related to urgency and leakage related to physical exertion. Mean ISI score for survivors with UI was 3.4 (SD = 3.0); scores ranged theri symptoms as moderate to very severe. Older age, but not postmenopausal status was significantly associated ($p < 0.05$) with UI severity. As expected, more severe UI was associated (p values <0.001) with greater distress on the UDI-6 and worse incontinence-specific quality of life in all domains on the IIQ-7.

Conclusion: These findingw suggest that UI symptoms are common in early BC survivors and that symptoms vary in severity from slight

to very severe. Findings also suggest that UI is associated with significant distress in survivors and may adversely impact survivors' physical, emotional and social functioning.
Disclosure of Interest: No significant relationships.

P295
QUALITY OF LIFE (QOL) AND CONCERNS IN BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT CHEMOTHERAPY

N. Odahara[1] *, K. Oda[2], T. Murata[2], Y. Sakakibara[3], S. Watanabe[3], A. Okada[3], M. Fujii[2], K. Akahane[2], S. Ando[4]. *[1]Department of Nursing, Nagoya University Graduate School of Medicine, Nagoya, Japan, [2]Breast Oncology, Aichi Cancer Center, Aichi Hospital, Okazaki, Japan, [3]Nursing, Aichi Cancer Center, Aichi Hospital, Okazaki, Japan, [4]Nursing, Nagoya University Graduate School of Medicine, Nagoya, Japan*

Goals: This study is aimed at clarifying the characteristic changes of QOL, concerns and depression (DP) of patients undergoing neoadjuvant chemotherapy (NAC), and identifying potential targets and opportunities for intervention to improve nursing care.
Methods: Among 81 patients diagnosed with breast cancer between December 2011 and September 2012, 30 consecutive patients with potential indications for NAC were enrolled in this prospective study. QOL was measured by QOL-ACD (Kurihara M, Psycho-Oncology, 1999) and QOL-ACD-B (http://csp.or.jp/qol/s3_3.pdf, accessed December 14, 2012). DP was measured by Distress and Impact Thermometer (DIT) (Akizuki N, J Pain Symptom Manage, 2005), and the concerns was measured by Cancer-chemotherapy Concerns Rating Scale (CCRS) (Kanda K, Japanese Society of Cancer Nursing, 2011). Patients were evaluated at the followings: In the patients receiving NAC (NACg), before the first course of chemotherapy (Ev. 1); before the second course of chemotherapy (Ev. 2); and before the fourth course of chemotherapy (Ev. 3). In the patients receiving radical operations (RO) followoed by adjuvant therapy (ROg), before the RO (Ev. 1); before the first course of chemotherapy (Ev. 2); before the second course of chemotherapy (Ev. 3); and before the fourth course of chemotherapy (Ev. 4).
Results: The number of patients in NACg and ROg was 9 and 20, respectively. Chemotherapy in NACg: EC (90/600mg/m^2); 1, FEC (100) followed by taxanes (T); 8. Adjuvant chemotherapy in ROg: FEC100 followed by T; 5, EC; 1, TC; 3, no adjuvant chemotherapy; 11.
NACg showed significantly lower scores of "concerns about financial problems" in QOL-ACD than ROg at treatment decision-making by the patients (Ev. 1) ($p < 0.01$). NACg also showed significantly more "social and economic concerns" in CCRS at Ev. 1 than Rog at Ev. 2 (before the first course of chemotherapy) ($p < 0.05$). "Social and economic concerns" in NACg interestingly decreased at Ev. 2 comparing to Ev. 1. There was a demographic subgroup of NACg showing higher "concerns of self existence" (CCRS) than the others, which tended to continue during NAC.
Conclusion: NAC patients frequently showed concerns on economic/financial problems, which might be caused by the expected expensive medical fee of NAC. It is necessary to develop effective psychosocial supports including detailed simulation of medical fee for the first course of chemotherapy for NAC patients at their treatment decision-making to reduce their concerns. Further analysis of the patients having continuous "concerns of self existence" is necessary to identify the cause and to develop effective interventions.
Disclosure of Interest: No significant relationships.

P296
INFLUENCE OF BREAST CANCER BIOLOGY ON POSTTHERAPEUTIC IMPAIRMENT AND REHABILITATION

H.G. Hass[1] *, T. Zabieglinski[1], V. Kunzmann[2]. *[1]Dept. of Oncology, Paracelsus Hospital, Scheidegg, Germany, [2]Dept. of Oncology, Hematology and Gastroenterology, University of Würzburg, Würzburg, Germany*

Goals: In contrast to patients with hormon-dependent (HDBC) or HER2neu positive breast cancer patients with so-called "triple negative" breast cancer (TNBC) had poorer prognosis with higher risk for tumor recurrence, lymph node involvement and metastasis. As a result of these observations TNBC patients were treated more intensive and often with mastectomy, lymph node resection or combined, aggressive chemotherapy. Less is known about specific adverse effects and individual impairments in relation to tumor biology and treatment and their importance for rehabilitation and quality of life.
Methods: Clinical and pathological data of 2000 patients with HDBC or TNBC who underwent oncologic rehabilitation between 2010 and 2012 in the Paracelsus Hospital in Scheidegg were documented in this retrospective unicenter study after informed and written consent.
Results: Actual the first data of 1180 analyzed patients were available for presentation. In 190 cases (16.1%) TNBC were noted, in 990 cases (83.9%) hormone-dependent (ER+/PR+) or Her2neu positive breast cancer. Mean age and were significantly different in women with TNBC compared with non-TNBC (52.8±22.5 vs. 56.7±19.7 years; $p = 0.02$). Especially in patients with TNBC tumors shows higher proliferative capacity (Ki67 47 vs. 15.5%; $p = 0.001$), poorer differentiation (G3 73.4 vs. 23.2%; $p = 0.001$) and an advanced tumor stage (>T1 48.8 vs. 36.2%; $p = 0.023$) or lymph node involvement (N+ 35.4 vs. 26.5%; $p = 0.02$). Treatment related follow-up impairments as lymph edema (15.2 vs. 11.7%; $p = 0.045$) or polyneuropathy (41.6 vs. 14.9%; $p = 0.001$) and duration of illness (until start of rehabilitation; 9.1 vs. 6.5 months, $p = 0.002$) were also seen more often in patients with TNBC.
Conclusion: Patients with TNBC not only had a poorer course of illness but also more treatment-related impairments during rehabilitation. These observations and a higher percentage of younger women with prolonged duration of illness underline the importance of oncological rehabilitation especially in these women with TNBC. These data may help to established more individual and focused rehabilitation concepts in specialized centers.
Disclosure of Interest: No significant relationships.

P297
COMPARISON OF QUALITY OF LIFE ACCORDING TO THE SURGICAL TECHNIQUES AMONG BREAST CANCER SURVIVORS

Y. Sun[1] *, E. Kang[1], C.Y. Heo[2], D. Kim[1], Y. Hwang[1], C.K. Yom[1], S.W. Kim[1]. *[1]Surgery, Seoul National University Bundang Hospital, Seongnam, South Korea, [2]Plastic Surgery, Seoul National University Bundang Hospital, Seongnam, South Korea*

Goals: Many breast cancer survivors have disabilities in physical and psychological aspect. Quality of life (QoL) has become a principal element in breast cancer treatment and study. In Korea, the median age of breast cancer patients in 2008 was found to be 49, more than a decade younger than that in Western countries. Therefore, QoL of the breast cancer survivor has even more significance in Korea where a rate of younger patients is high. Thus this study aims to assess differences in QoL among the breast cancer survivors.
Methods: The cross-sectional study was conducted during the follow-up visits. Women at least 2 years after surgical treatment were eligible if patients were between age 20 and 69, and had a diagnosis of breast cancer (stage 0–III). QoL was evaluated based on the Korean version of the EORTC QLQ-C30, EORTC QLQ-BR23,

Rosenberg self-esteem scale (RSES), Beck depression index (BDI), body image scale (BIS), and sexual scale of cancer rehabilitation evaluation system (CARES).

Results: A total of 407 patients were included in the analysis. The breast conserving surgery (BCS) was performed in 254 (62.4%) women and 122 (30%) women underwent the total mastectomy (TM) whereas 31 (7.6%) women underwent the immediate reconstruction after total mastectomy (TM-R). The mean age was 51.6 years old (range, 28–70 years). The mean period from the surgery to the survey was 49 months (range, 24–104 months). The clinical characteristics by surgical treatment groups had significantly differences in age, stage, chemotherapy, and radiotherapy. The scores of questionnaires adjusted by age, mean follow-up period since the surgery, stage, chemotherapy, radiotherapy, and hormone therapy. Women in the BCS group showed better outcomes than TM and TM-R group in emotional-social function, nausea/vomiting, and financial difficulty in EORTC QLQ-C30, body image and arm symptom in EORTC QLQ-BR23. Also, the BCS group presented better outcome in RSES. BIS, and Sexual satisfaction of CARES. There are a few differences in emotional function, nausea/vomiting, and arm symptom between TM group and TM-R group, but TM and TM-R group showed similar QoL.

Conclusion: According to long term follow-up, it appears that QoL was better in BCS group compared to TM or TM-R group. Effort to improve QoL of patients with breast cancer who were treated with total mastectomy should be continued.

Disclosure of Interest: No significant relationships.

P298

SYMPTOMS, CLUSTER SYMPTOMS AND QOL AMONG BREAST CANCER SURVIVORS COMPARED TO HEALTHY WOMEN

T. Mekel Modiano[1] *, B. Kaufman[1], S. Paluch Shimon[1], M. Shabtai[2], D. Pud[3]. *[1]Oncology, Sheba Medical Center, Ramat Gan, Israel, [2]Surgery, Sheba Medical Center, Ramat Gan, Israel, [3]Nursing, University of Haifa, Haifa, Israel*

Goals: Over 80% of women diagnosed with breast cancer will survive the disease and yet studies demonstrate that many will continue to experience multiple symptoms such as fatigue, pain, depression and sleep disturbance for years after diagnosis. Clustering of symptoms is a method used to categorize two or more symptoms occurring simultaneously and associations exist between cluster symptoms and quality of life (QOL). Our study assessed prevalence and severity of cluster symptoms and the associated impact on QOL amongst Israeli breast cancer survivors.

Methods: 59 breast cancer survivors who were one year post-completion of adjuvant treatment and a control group of 43 healthy women were included. Participants completed questionnaires using established and validated tools assessing distress, severity, and frequency of symptoms, fatigue, sleep disturbances, depression, and pain intensity. Functional QOL and general QOL were measured for the survivor group. Cluster analysis was conducted to identify clusters symptoms.

Results: Among survivors, symptoms of fatigue, pain, depression and sleep disturbance were significantly higher compared to the control group (p-value <0.001 for each of the symptoms). Three clusters of symptoms were identified among survivors and categorized from low to high intensity of all symptoms. 39% of the survivors belonged to the "low cluster", 37.3% to the "Moderate cluster", and 23.7% to the "High cluster". In the control group, only 2 cluster symptom subgroups were identified: a low (56%) and moderate (44%) cluster. Significant differences in functional QOL were found between survivors and the controls. Of the 32 symptoms assessed, eight symptoms occurred more frequently among survivors (sleep difficulties, anxiety, lack of energy, pain, stress, nervousness, bloating and sadness). There were a strong negative correlation between the average distress caused by these symptoms and general QOL and functional QOL ($r = -0.51$, $p < 0.01$, $r = -0.47$, $p < 0.001$ respectively). Thus, higher levels of distress caused by the symptoms were associated with lower QOL, and vice versa.

Conclusion: Our study demonstrates that many breast cancer survivors will suffer from a significantly higher level of cluster symptoms and lower QOL than healthy women. Our findings highlight the importance of assessing symptoms and QOL amongst breast cancer survivors and the need for further research into the etiology of these symptoms and effective interventions.

Disclosure of Interest: No significant relationships.

P299

SYMPTOMS OF POSTTRAUMATIC STRESS IN NEWLY DIAGNOSED BREAST CANCER PATIENTS: A PROSPECTIVE STUDY

G. Bulotiene[1] *, J. Matuiziene[2], V. Ostapenko[3]. *[1]Physical Medicine and Rehabilitation, Institute of Oncology, Vilnius University, Vilnius, Lithuania, [2]University of Applied Sciences, Vilnius, Lithuania, [3]Vilnius University, Institute of Onccology, Vilnius, Lithuania*

Goals: This research is part of a larger study investigating predictors of the negative psychosocial outcomes that could be used in clinical practice to risk-assess and monitor breast cancer patients for adjustment difficulties. The present study aimed to identify the prevalence of posttraumatic stress and its association with clinical and social factors in newly diagnosed early breast cancer patients.

Methods: One hundred thirty five newly diagnosed early breast cancer patients completed four questionnaires: Impact of Event Scale – revised (IES-R), Beck Depression Inventory II (BDI-II), Beck Scale for Suicide (BSS), Vrana & Lauterbach Traumatic Events Scale-Civilian (TEQ). Women were questioned before surgery in Institute of Oncology Vilnius University.

Results: 34% of newly diagnosed breast cancer patients had no any symptoms of posttraumatic stress. 37% of the patients had moderate to severe symptoms of this disorder (score average of IES-R questionnaire was 2 and more). 39% of the women were suffering from depression of different level. Factors associated to high scores of posttraumatic stress are depression (0.63; $p < 0.001$), earlier and present psychological traumatic experience (0.43; $p < 0.01$). A significant association was found between cancer stage and avoidance symptoms of posttraumatic stress (0.34; $p < 0.004$) and between living place and hyper arousal symptoms of posttraumatic stress (0.3; $p < 0.006$), patients living in rural district had more of these symptoms. Patients who indicated that they have sad mood and are pessimistic had more avoidance symptoms of posttraumatic stress disorder (0.36; $p < 0.000$). A negative correlation was found between manifestation of posttraumatic stress disorder and time, which passed from the moment patients were informed that they are ill with the breast cancer (−0.33; $p < 0.01$).

Conclusion: Significant numbers of breast cancer patients suffer psycho emotional problems. The finding show that early evaluation of psycho emotional needs of breast cancer patients is necessary and early psychological interventions are meaningful especially if patient states about traumatic experience, bad mood or often episodes of crying.

Disclosure of Interest: No significant relationships.

P300

EFFICACY OF SCALP COOLING TO PREVENT HAIR LOSS IN BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY

T. Kinoshita[1] *, K. Tamura[2], A. Hashimoto[2], S. Arai[3], Y. Ryushima[3], M. Asanabe[4]. *[1]Division of Breast Surgery, National Cancer Center Hospital, Tokyo, Japan, [2]Division of Breast and Medical Oncology, National Cancer Center Hospital, Tokyo, Japan, [3]Pharmacology, National Cancer Center Hospital, Tokyo, Japan, [4]Oncology Nurse, National Cancer Center Hospital, Tokyo, Japan*

Goals: Chemotherapy is often used to treat breast cancer patients both pre- and post-surgically. Cyclophosphamide, Anthracycline and

taxane agents are most commonly used, with hair loss, nausea, vomiting, numbness, and fever as side effects. Nausea, vomiting, and fever can be treated pharmacologically, but since there are no preventive measures for hair loss, only symptomatic therapies such as the use of wigs or hats, hair loss significantly reduces patients' quality of life (QOL). Hospital departments must improve their cooperation with each other in order to confirm the efficacy of hair loss prevention and the safety of scalp cooling equipment, and thus enhance patient recovery and QOL.

Methods: This study used scalp-cooling equipment (Paxman Cooler, U.K.) from the United Kingdom, and targeted female breast cancer patients scheduled to receive 4 cycles of postoperative adjuvant chemotherapy using either AC (60/600 mg/m^2) or TC (75/600 mg/m^2). The primary outcome was the proportion of patients able to complete 4 cycles of postoperative adjuvant AC or TC therapy. Secondary outcomes were the degrees of comfort, satisfaction, and hair loss prevention, as well as the rates of adverse events and metastases to the scalp in patients who used the scalp cooling equipment.

Results: At the time of this writing we had evaluated 21 cases: 11 who received AC therapy and 10 who received TC therapy. Protocol completion rates were 81.8% (9 cases) for AC therapy and 100% (10 cases) for TC therapy. Hair loss was graded using the WHO classification scheme; the numbers of cases for each Grade from 0–4, respectively, were 0, 3, 2, 5, and 1 during AC therapy, and 0, 3, 3, 4, and 0 for TC therapy. A wig is not considered necessary for hair loss up to Grade 2. The proportion of patients with Grade 1–2 hair loss was 5/11 cases (45.5%) in the AC group, and 6/10 cases (60%) in the TC group, or 11/21 cases (52.4%) overall. Furthermore, scalp cooling resulted in greater hair loss prevention during TC therapy than AC therapy. Two patients could not complete the protocol treatment, 1 due to headaches and 1 due to chills. These patients discontinued the scalp cooling procedure and had Grades 3 and 4 hair loss, respectively. In the questionnaire survey following completion of the protocol, 15 of 21 (71.4%) patients responded that they would "strongly recommend the same treatment to others."

Conclusion: We will continue studying the effects of scalp cooling in breast cancer patients undergoing chemotherapy, and work to improve on the design of the original scalp cooling equipment. Our goals are to develop a hair loss prevention system that is effective enough to be implemented at clinical sites and in turn, can also increase patient satisfaction and QOL.

Disclosure of Interest: No significant relationships.

P301

THE DIGNICAP™ SYSTEM TO PREVENT ALOPECIA IN WOMEN RECEIVING CHEMOTHERAPY FOR BREAST CANCER

H.S. Rugo[1] *, K. Serrurier[2], M. Melisko[1], A. Glencer[2], J. Hwang[2], R. D' Agostino[3], S. Hutchens[3], L. Esserman[2], S. Melin[3]. [1]*Department of Medicine, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, United States of America,* [2]*University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, United States of America,* [3]*Wake Forest University Baptist Medical Center, Winston-Salem, United States of America*

Goals: Alopecia is a non-life threatening complication of adjuvant chemotherapy (CTX) for early stage breast cancer (BC). CTX induced hair loss affects quality of life and potentially impacts decisions regarding the risks and benefits of treatment. Scalp cooling (SC), used internationally by thousands of patients (pts) including a growing number in the U.S., is thought to prevent hair loss through decreased follicular metabolic rate and vasoconstriction resulting in reduced delivery and cellular uptake of drugs. The DigniCap™ System is a self-contained SC system with circulating coolant. We sought to evaluate feasibility and efficacy of the DigniCap™ System in pts with stage I BC.

Methods: We performed an initial prospective feasibility study before a planned pivotal trial. The primary endpoint was feasibility, defined as <50% of pts discontinuing cap use due to cap-associated toxicity. Secondary endpoints included prevention of hair loss (HL) assessed by an independent panel (IP) consisting of a hairdresser, patient advocate, and dermatologist using photographs taken from 5 angles and blinded to pt and CTX cycle using the 5 point Dean's scale for HL: grade 0 (no HL), 1 (<25% HL), 2 (25–50% HL), 3 (50–75% HL), and 4 (>75% HL). Pts assessed their own HL using the Dean's scale, and pt-assessed quality of life, time to and quality of hair re-growth, and impact of HL on treatment decisions were also evaluated. Successful prevention of alopecia was defined as <grade 2 HL by the Dean's scale. Eligibility included stage I disease and excluded use of anthracycline-taxane combination or sequential CTX.

Results: 20 pts were enrolled. CTX regimens included: docetaxel and cyclophosphamide (TC) × 4–6 cycles (n = 16), weekly paclitaxel and trastuzumab ×12 (n = 2), and docetaxel, carboplatin, and trastuzumab (TCH) x 6 (n = 2). 19 of 20 pts (95%) completed all CTX using the DigniCap™ System. By IP assessment, 15 pts (75%) had a maximum of <grade 2 HL; 2 pts (10%) and 3 pts (15%) had a maximum grade 3 or 4 HL respectively. By pt assessment, 11 pts (55%) reported <grade 2 HL. 68% and 32% of pts reported grade 1 or 2 toxicity, respectively, including head/scalp pain, feeling chilled, and rash. 85% of pts reported that SC made decisions about CTX easier. At a median follow-up of 20 months, no scalp metastases have been observed.

Conclusion: Use of the DigniCap™ System is feasible, effective in preventing CTX-induced alopecia in the majority of users, and safe with short-term follow-up in pts with stage I BC. Additional studies should help to define potential causes for cap failure. This is the first prospective US trial to evaluate the effect of SC using an expert IP and blinded photographs to assess extent of alopecia. A larger trial is planned to confirm these results in pts with stage I/II disease. Support for this trial was provided by the Tauber Foundation (UCSF), the Madonia and Cooper Funds (WFBH), and Dignitana.

Disclosure of Interest: Dr. Rugo has received travel support from Dignitana. The Dignicap System was provided by Dignitana to the University of California and Wake Forest University for the purpose of this study.

P302

THE INFLUENCE OF TAMOXIFEN ON EMOTIONAL AND COGNITIVE FUNCTIONS

Y.V. Malova *. *Psychological Faculty, Lomonosov Moscow State University, Moscow, Russian Federation*

Goals: The present study examines effects and discusses possible mechanisms of mood and coping disorders in patients treated with tamoxifen. The patients' self-reports as well as psychological assessments expose major undesirable effects of tamoxifen treatment, such as difficulties in coping with the cancer and its treatment and secondary family problems. Estrogen is supposed to play a significant role in emotional modulation and short-term memory.

Methods: One hundred records of breast cancer patients requiring psychological help were examined, focusing on difficulties in coping, short-term memory assessments, anxiety level diagnostics and evidence of depressive disorders. The mental characteristics of twenty tamoxifen-treated (TT) receptor-positive patients were compared with those of a matched group of patients with receptor-negative tumors (TF patients).

Results: Of the patients with coping problems needing long-term psychological support, a significant majority were TT patients. In addition, TT patients had significantly lower scores for short-term memory, more dysthymia and more anxious-depressive disorders than TF patients.

Conclusion: Antagonists of the estrogen receptors have detrimental effects on learning and coping, as well as on the restoration of coping by psychotherapy and on general rehabilitation.
Disclosure of Interest: No significant relationships.

P303
APPLICATION OF THE PEARLIN STRESS PROCESS MODEL IN MALE CAREGIVERS OF BREAST CANCER PATIENTS

S. Dihmes, M. Habibi*, M. George, S. Jarvandi. *Johns Hopkins Bayview Breast Center, Johns Hopkins University School of Medicine, Baltimore, MD, United States of America*

Background: The number of cancer patients receiving informal care at home is at an all-time high (National Alliance for Caregiving & AARP, 2009). As a consequence of cancer survivorship, more men are serving as primary caregivers to their wives, mothers, and relatives with this chronic illness (Golant & Haskins, 2008). The National Center on Caregiving reports that 65.7 million Americans (29% of the U.S. adult population) have a family member delivering informal caregiving to a loved one (2012). Cancer is detrimental to not only the patient, but also their spouse and family (Carey et al., 1991; Given et al., 1993; Jansen et al., 1993). Individuals who are giving care to a loved one are susceptible to becoming psychologically, physically, socially and financially distressed from the responsibility. The National Family Caregivers Association reported that in 2000, 61% of caregivers suffered from depression, reiterating the severity of caregiver burden (Kinsella et al., 1998; Parks & Pilisuk, 1991). Detecting and treating stress from caregiving before it develops into clinical depression is essential to both caregiver and patient. When a caregiver's mental health is compromised, the quality of care they deliver to the patient is also at risk. The majority of caregiving research only focuses on female caregivers. Of the research that has focused on men as caregivers, most of the studies are on Alzheimer's disease and dementia; thus the research on male caregiving does not include disease-specific stressors that accompany caring for a loved one with cancer (Black et al., 2008; Fuller-Jonap & Haley, 1995). Lastly, the field of male caregiving is incomplete because much of the research regarding men's involvement as cancer caregivers focuses on aged husbands (Chang et al., 1999; Gilbar, 1999). This field can be broadened by including working-age men who care for their loved ones with cancer.
Objective: This study will focus on male caregivers delivering care to their loved ones who carry the diagnosis of breast cancer, which has the highest incidence of cancer in U.S. women (National Cancer Institute, 2011).
Methods: We recruited male caregivers (N = 65) and surveyed them about their stressors and symptoms of distress. We submitted all variables of the Adapted Stress Process Model to a Stepwise Multiple Regression analysis to examine the overall association of primary and secondary stressors with male caregiver stress outcome and determine the best predictors of caregiver stress. We used Baron and Kenny's (1986) procedure for estimating mediational effects using a series of regression analyses. As recommended by Baron and Kenny, the Sobel test was used to determine if the reduction in prediction was statistically significant.
Results: It was found that marital satisfaction and shame partially mediate the relationship between role strain and both physical and mental health status. All statistical assumptions were satisfied for the regression analysis.
Conclusions: Caregiver's age, role strain, depression symptoms, and health status along with breast cancer patients' functional level can predict outcome of male caregivers' well-being. Male caregivers should be screened for high role strain, as an increase in this area is correlated with lowered psychological and physical health. Interventions that help men cope with shame and interventions that assist couples coping with relationship issues should also be offered since they have an impact on the level of men's depression symptoms.

Reference(s)

Baron, R.M. & Kenny, D.A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 51, (6), 1173–1182.
Black, H.K., Schwartz, A.J., Caruso, C.J., & Hannum, S.M. (2008). How personal control mediates suffering: Elderly husbands' narratives of caregiving. *The Journal of Men's Studies*, 16(2), 177–192.
Carey, P.J., Oberst, M.T., McCubbin, M.A., & Hughes, S.H. (1991). Appraisal and caregiving burden in family members caring for patients receiving chemotherapy. *Oncology Nursing Forum*, 18(8), 1341–1348.
Chang, H.Y., Chiou, C.J., & Chen, N.S. (1999). Impact of mental health and caregiver burden on family caregivers' physical health. *Archives of Gerontology and Geriatrics*, 50(3), 267–271.
Fuller-Jonap, F., & Haley, W.E. (1995). Mental and physical health of male caregivers of a spouse with Alzheimer's disease. *Journal of Aging and Health*, 7(1), 99–118.
Gilbar, O. (1999). Gender as a predictor of burden and psychological distress of elderly husbands and wives of cancer patients. *Psychooncology*, 8(4), 287–294.
Given, C.W., Stommel, M., Given, B., Osuch, J., Kurtz, M.E., & Kurtz, J.C. (1993). The influence of cancer patients' symptoms and functional states on patients' depression and family caregivers' reaction and depression. *Health Psychology*, 12(4), 277–285.
Golant, M., & Haskins, N.V. (2008). "Other cancer survivors": the impact on family and caregivers. *The Cancer Journal*, 14(6), 420–424.
Jansen, C., Halliburton, P., Dibble, S., & Dodd, M.J. (1993). Family problems during cancer chemotherapy. *Oncology Nursing Forum*, 20(4), 689–694; discussion 694–686.
Kinsella, G., Cooper, B., Picton, C., & Murtagh, D. (1998). A review of the measurement of caregiver and family burden in palliative care. *Journal of Palliative Care*, 14(2), 37–45.
National Alliance for Caregiving & AARP. (2009). *Caregiving in the U.S.*. Retrieved November 15, 2010 from the National Alliance for Caregiving Web site: http://www.caregiving.org/data/Caregiving_in_the_US_2009_full_report.pdf
National Cancer Institute. (2011). *Breast Cancer.* National Cancer Institute Website. Retrieved January 5, 2011, from http://www.cancer.gov/cancertopics/types/breast.
National Center on Caregiving: Family Caregiver Alliance. (2012). *Selected caregiver statistics.* Retrieved January 1, 2013, from http://www.caregiver.org/caregiver/jsp/content_node.jsp?nodeid=439.
Parks, S.H., & Pilisuk, M. (1991). Caregiver burden: gender and the psychological costs of caregiving. *American Journal of Orthopsychiatry*, 61(4), 501–509.

Disclosure of Interest: No significant relationships.