

counterparts. Higher levels of androgenic hormones in Indian breast cancer patients may have etiological and therapeutic implications.

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POSTER

# **Non-pegylated Liposomal Doxorubicin (Myocet®) Plus Docetaxel (Taxotere®) (MYTAX), as First-line Chemotherapy (CHT), in Metastatic Breast Cancer (MBC): Results of a Phase II Study**

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**Background:** The combination of anthracyclines and taxanes is considered among the most effective treatments in MBC. The main limitation of these regimens is the cumulative cardiotoxicity of anthracyclines. The liposomal doxorubicins have been demonstrated to be less toxic for myocardial tissue, resulting in a better cardiac safety profile.

**Purpose:** We report our experience regarding efficacy and safety of the combination of Myocet® with Taxotere® in first-line treatment of MBC patients (PTS).

**Patients and Methods:** All 16 PTS with median age of 61 years (range 54–75), had histologically confirmed MBC. Anti-allergic premedication with steroids and H1/H2 receptor antagonists was administered to all PTS 12 hours before Taxotere®.

Treatment plan was: Myocet® (60 mg/m<sup>2</sup>, i.v. on day 1) followed by Taxotere® (35 mg/m<sup>2</sup> i.v. on days 2 and 9), every 3 weeks.

A total of 92 cycles of CHT were delivered. Mean number was 5.75 (range 2–8). Seventy-six percent of PTS received at least 6 cycles of CHT.

The primary endpoint was overall response rate (ORR), whilst time to progression (TTP) and safety were considered as secondary end points.

**Results:** According to the WHO criteria, 3 PTS (18.5%) achieved a complete remission and 4 (25%) a partial remission for an ORR of 44%. We report a median TTP of 9.5 months. Two patients who achieved RC had lymph nodal disease, one patient had liver disease. None of the PTS experienced severe cardiac toxicity. The most common hematological toxicity was grade 3–4 neutropenia, according to WHO criteria, detected in 68% of PTS. Use of G-CSF, in 55% PTS, for treatment and prophylaxis of severe neutropenia allowed to maintain adequate dose-intensity. Stomatitis occurred in 25% of PTS, while grade 3 neurological toxicity in 12.5%.

**Conclusions:** Our report confirms the effectiveness of the Myocet®-Taxotere® combination administered in MBC according to the schedule described above. Moreover the substitution of conventional doxorubicin with Myocet® probably reduced cardiotoxicity. Myelotoxicity rate is in line with other similar reports.

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POSTER

# **Phase II Study of Vinorelbine Plus Trastuzumab in HER-2 Overexpressing Metastatic Breast Cancer Pretreated With Anthracyclines and Taxanes**

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**Background:** The role of first-line trastuzumab-based therapy has been firmly established in HER-2 positive metastatic breast cancer patients. In this trial, we evaluated the efficacy and safety of a vinorelbine and trastuzumab combination chemotherapy failed to anthracyclines and taxanes.

**Methods:** Thirty-three patients with HER-2 overexpressing metastatic breast cancer, all of whom had previously been treated with anthracyclines and taxanes, were included in this study. The patients were treated with 25 mg/m<sup>2</sup> of vinorelbine (over a 15-minute infusion) on days 1 and 8 every 3 weeks. Additionally, trastuzumab was administered at an initial dose of 4 mg/kg over 90 minutes, and was subsequently administered at weekly doses of 2 mg/kg (over 30 minutes).

**Results:** The median age of the patients was 53 years (range: 39–72 years). The overall response rate was 30.3% (10 patients, 95% confidence interval [CI]: 23–57%). The median time to progression was 6.8 months (95% CI: 5.3–8.2 months). The median overall survival was 12.4 months (95% CI: 10.3–14.6 months). In the 194 cycles of treatment, the incidence rates of grade ≥ 3 neutropenia and anemia were 7.2% and 1.0%, respectively. Neutropenic fever was detected in 3 cycles (1.5%). The non-hematological toxicities were not severe: grade 1 or 2 nausea or vomiting was detected in 15.2%, and grade 2 neuropathy was noted in 6.1% of the patients. None of the patients experienced any serious cardiac toxicity, and no treatment-related deaths occurred.

**Conclusions:** These results show that a combination chemotherapy consisting of vinorelbine and trastuzumab is useful in HER-2-overexpressing metastatic breast cancer patients failed to anthracyclines and taxanes, with a favorable toxicity profile.

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POSTER

# **Inflammatory Breast Cancer (IBC): Does the Confirmation of Dermal Lymphatic Invasion (DLI) Predict the Worst Outcome?**

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**Background:** IBC presents the most aggressive form of BC, with poor prognosis and low rate of complete remission to induction chemotherapy (iCT). Dermal lymphatic invasion (DLI), although not necessary for IBC diagnosis, is identified in fewer than 75% patients, mainly because of sampling heterogeneity. The aim of this retrospective analysis is to evaluate if DLI is related to poorer prognosis, by comparing two groups of IBC patients: with and without confirmed DLI.

**Materials and Methods:** At Institute for oncology and radiology of Serbia (IORS), in period 2008–2010, we have registered 98 female pts with IBC stage III. 85 medical records were available for evaluation. IBC is defined as BC with typical clinical signs of cancer-mastitis, with or without pathologically confirmed skin lymphangiosis and with or without underlying tumour.

**Results:** The incidence of IBC at IORS is 2.8%. There were 40pts (47%) with confirmed DLI and 45pts (53%) without DLI at skin biopsy.

	Pts, % (n)	CR/PR to iCT	PD to iCT	PD (pts)	TTP	Died	OS
With DLI	47% (40)	55%	35%	40%	12.8 mo	10%	12.5 mo
Without DLI	53% (45)	75%	13%	22%	14.8 mo	4%	20 mo

In these two groups the median age at diagnosis was 54.7 years (range 34–76) and 56.8 years (range 28–77), respectively. Pathohistological analysis confirmed ductal carcinoma in 35% (14pts) and 64.5% (29pts); underlying tumour in 72.5% (29pts) and 93.5% (42pts); ER+ 57.5% (23pts) and 31% (14pts); HER2+ 50% (20pts) and 46.5% (21pts). Good clinical response to induction chemotherapy, estimated as complete (CR) or partial response (PR) was registered in 55% (22 pts) and 75% (34pts); stable disease (SD) in 10% (4pts) and 11% (5pts), while 35% (14pts) and 13% (6pts) failed to respond to iCT (PD), all respectively. Median time to progression (TTP) was 12.8 and 14.8 months, registered in 40% (16pts) and 22% (10pts). In a group of pts with confirmed DLI 4pts (10%) died, compared to 2pts (4%) in group without confirmed DLI, with overall survival (OS) respectively 12.5 and 20 months.

**Conclusions:** In this study we showed that IBC pts with confirmed DLI have worse outcome, including lower response rate to iCT (55% vs. 75%) and more common disease progression (40% vs. 22%) with shorter TTP (12.8 vs. 14.8 months) and OS (12.5 vs. 20 months). We also found that DLI in IBC is associated with more frequent ER positivity (57.5% vs. 31%) and absence of underlying tumour (27.5% vs. 6.5%).

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POSTER

# **Polymorphisms in Genes Involved in Drug Detoxification and Response to Anthracyclines Chemotherapy in Chinese Han Breast Cancer Patients**

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**Background:** Chemotherapy drug efficacy is complex and can be influenced by cellular detoxification mechanisms involving drug metabolism and transport pathways. This study aimed to assess whether the known polymorphisms in genes related to metabolizing enzymes (MnSOD, CAT and GSTs) and transporter MDR1 are associated with response to anthracycline-based chemotherapy in Chinese Han breast cancer patients.

**Materials and Methods:** Genotyping was performed by allele-specific oligonucleotide ligation reaction (MnSOD, CAT, GSTP1), multiplex PCR (GSTM1, GSTT1), and PCR-RFLP (MDR1). Based on 153 evaluable patients received anthracycline-based neoadjuvant chemotherapy, the associations of these genotypes, their combinations or their haplotypes with clinical responses were analyzed.

**Results:** Patients with GSTP1 313 AA genotype had inferior response rates relative to those with AG or GG (58.4% vs 77.8% or 100.0%;  $\chi^2=4.922$ ,  $P=0.027$ ); Moreover, the response rate of the combination of GSTP1 AA with both GSTT1 and GSTM1 present was 44%, which was also lower comparing with the other groups (70.3%;  $\chi^2=6.454$ ,  $P=0.011$ ). A similar result was noticed for MDR1 3435 TT genotype, which had a significantly worse chemotherapy response compared with wild-type C allele carrier (33.3% vs 71.2%;  $\chi^2=11.586$ ,  $P=0.001$ ); Further, the

response rate of the patients with 3435T-2677T, 3435T-1236T or 3435T-2677T-1236T haplotypes was lower than that of the patients with the other corresponding haplotypes ( $P = 0.018$ ,  $0.011$  and  $0.019$ , respectively), too. Noticeably, the patients with both the adverse genotypes of *GSTP1* 314AA and *MDR1* 3435TT shown the worst treatment efficacy in all (14.3%;  $\chi^2 = 26.33$ ,  $P = 0.000$ ).

**Conclusion:** Polymorphisms in *GSTs* and *MDR1* genes may help to predict anthracyclines response, but further validation is required. These results provide support for a polygenic pathway approach for assessing the predictive potential of polymorphisms in treatment outcome.

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## POSTER

### The Substantiation of Optimal Approaches to Systemic Treatment for Patients With Metastatic Breast Cancer

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Breast cancer is one of the most common malignancies in the US and Europe. Our work is directed on the decision of actual clinical problem in oncology. The investigation aimed to improve the results of systemic treatment for patients with metastatic breast cancer. It is reached via consideration of optimal chemotherapy duration, elaboration of indications and contra-indications for continuation or termination based on defining factors, which influence on total and recurrence-free patients' survival.

**Patients and Methods:** 128 women with histologically confirmed metastatic breast cancer, received monotherapy with Paclitaxel 80 mg/m<sup>2</sup> weekly. Patients (Pts.) were divided for 2 groups. First group consists of 61 pts. received chemotherapy during 24 weeks. Second group included 67 Pts. received chemotherapy without limitation term of treatment.

**Results:** Treatment of patients on the stage of 24 weeks were identical in both groups and corresponded to the known international data. Continuation of treatment from 24 to 48 weeks improved the results of of tumour response on 27.5%. Thus treatment appeared most optimal duration 40 weeks.

The following results in both groups have been found. The patients with liver and lymph nodes lesions who have stable disease response at week 24 should stop the treatment. If the response is partial the treatment may be prolonged up to 32 weeks. If the partial response grows and preserves at week 32 the treatment may be prolonged till week 40 and must be stopped. If the partial response does not grow 32 week term of treatment is sufficient. The patients with breast cancer with liver or liver and lung localized metastases who have objective treatment response are recommended to be treated up to 48 weeks (if possible). Only if the partial response growth is preserved after 48 weeks at the last control time interval uninterrupted treatment may benefit. If the partial response is stable the treatment may be terminated.

**Conclusions:** Taking into account the substantial differences of efficiency depending on duration of chemotherapy, necessary selection of patients for it's continuation. Testimonies to continuation of treatment were the next: presence of metastases in a liver maintenance of partial tumour response on treatment and it's increase for the last controlled interval of time.

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## POSTER

### Association Between Some Markers ( $\beta$ -Tubulin III, Tau-1, BRCA-1, DPD, TP, TS) and Treatment Response in Patients With Advanced Breast Cancer

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**Background:** The main purpose of our study was to find substitute predictive markers for treatment response in women with advanced breast cancer.

**Materials and Methods:** 39 patients with advanced breast cancer, treated in the St. Petersburg Research Institute of Oncology between 2007 and 2009 were included in this trial. 20 patients received docetaxel 75 mg/m<sup>2</sup> i.v. once every three weeks and 19 patients were treated with capecitabine 2500 mg/m<sup>2</sup> per os. We compared the expression of BRCA-1,  $\beta$ -tubulin, and tau-1 in the 20 patients treated by docetaxel between those with a good overall response (stable and partial) and patients with a progression of disease. In the group including 19 patients we compared the expression of DPD, TP and TS between the same response subgroups.

**Results:** A low expression of BRCA-1,  $\beta$ -tubulin, and tau-1 in patients receiving docetaxel correlated with a worse response. Among the patients receiving capecitabine a low expression of DPD, TP, and TS correlated with a good response.

**Conclusion:** These results demonstrate that BRCA-1,  $\beta$ -tubulin and tau-1 may be substitute markers for patients receiving docetaxel. DPD, TP and TS may be markers among patients receiving capecitabine.

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## POSTER

### ABO and Rh Blood Groups Frequency in Women With HER2(+) Breast Cancer

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**Background:** The role of genetic factors in the development of cancer is widely accepted. In 1953 Aird et al. reported a relation between blood group A and cancer of the stomach. Recently the relation between pancreatic cancer and ABO blood group has been described. It is well known that genetic factors (e.g. BRCA1/2) are involved in the etiology of some cases of familial breast cancer. ABO blood group genes are mapped at the chromosome 9q, in which the genetic alteration is common in many cancers. Individualized current therapeutic strategies for patients with primary breast cancer are frequently determined by the size of the primary tumour, axillary lymph node status, and pathologic stage of disease, status of estrogen receptor and progesterone receptor activity and HER2 over expression. In some previous studies, investigators have recognized ABO blood group as a predisposing or prognostic factor in breast cancer. The aim of this study is to investigate the presence of a possible association between HER2(+) breast cancer in Turkish women and ABO blood groups and Rh factor.

**Material and Methods:** In 294 female patients with HER2(+) breast cancer, blood group and Rh factor were examined. the relationship of blood groups with age, menopausal status, family history of cancer, ER, PR and HER2 status were evaluated and compared with the healthy volunteer donors control group of 22,821 people which admitted to Ankara University Medical School Blood Center at 2010.

**Results:** Information on ABO blood type and Rh factor were available for 294 patients. The median age was 47 (range: 20-80) and 56% of patients were at premenopausal period. Estrogen and progesterone receptor were positive 50% and 60% respectively. Overall, the ABO blood group distribution of the 294 HER2(+) breast cancer patients was similar to that of the Turkish general population. There wasn't statistically significant difference ( $p = 0.36$ ) between groups (see Table 1). Also blood type and ER, PR and menopausal status was not correlated. However, patients with blood group A and 0 Rh(+) had higher family history of cancer ( $p = 0.04$ ).

**Conclusion:** In the present study we didn't find any relationship between HER2 status and ABO blood group and Rh factor. However further studies with larger number of patients are needed to establish the role of blood groups as a prognostic factor in patient with breast cancer.

Table 1: The blood group distribution of patients and control group

Blood group	Number of subjects			
	HER2(+) patients		Controls	
	n	%	n	%
A Rh(+)	135	45.8	8795	38.54
A Rh(-)	10	3.4	1130	4.95
B Rh(+)	37	12.6	3185	13.96
B Rh(-)	5	1.7	425	1.86
AB Rh(+)	19	6.5	1581	6.93
AB Rh(-)	2	0.7	205	0.90
O Rh(+)	77	26.2	6550	28.70
O Rh(-)	9	3.1	950	4.16
Total	294	100	22821	100

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## POSTER

### Identification of Protein Markers Predicting Chemotherapy Resistance in Breast Cancer

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**Background:** Metastasis and subsequent resistance to therapy is a major cause of death in patients with breast cancer. Although a large number