**433** PUBLICATION

**A Phase II study of neoadjuvant chemotherapy (NC) with taxotere, adriamycin and cyclophosphamide (TAC) in locally advanced breast cancer (LABC)**

A. Lal, A. Alidina, I. Vaziri. *Aga Khan Hospital University, Medical Oncology, Karachi, Pakistan*

**Background:** NC is the standard treatment for LABC. The objective of this study is to determine the response rates and the rates of breast conservation therapy with NC containing TAC in LABC.
**Methods:** Women were eligible if they were; histological confirmed invasive infiltrating carcinoma, LABC as per AJCC. PS 0–1 with adequate renal, liver and hematological functions. Patients were treated with T (75 mg/m$^2$), A (50 mg/m$^2$) and C (500 mg/m$^2$) 3 to 6 cycles. Followed by surgery and pathological assessment. The post-surgical treatment cycles of TAC regimen and radiotherapy is given on the basis of staging. Tamoxifen was given if they were found hormonal receptors positive.
**Results:** We have accrued 60 patients with mean age 46 years; 45% were premenopausal; 55% had T3, 25% had T4, while 20% had inflammatory breast cancer. Seventy percent had clinically/mammographically positive axillary lymphadenopathy. Hormonal receptors were positive in 53%. The overall response rate in all 60 pts was 93% with complete pathological response (pCR) in 28.3% and partial response (PR) in 65%. Disease progression was seen in one patient. Grades III-IV toxicities were: neutropenic fever 35%; mucositis 45%, and nausea & vomiting 10%. All patients were operated, 65% had a modified radical mastectomy and 35% had BCT.
**Conclusions:** Neoadjuvant chemotherapy containing Taxotere, Adriamycin and Cyclophosphamide achieved significant pathological complete response and breast conservation therapy in patients with locally advanced breast cancer.

**434** PUBLICATION

**Efficiency of Toremifene and Letrozole in the treatment of patients with advanced breast cancer**

R. Zeynalov, I. Musayev, S. Giyasbeyli, N. Dadasheva, J. Gasanzadeh, A. Yusifov, N. Ahadova. *Oncologic research center, department of chemotherapy, Baku, Azerbaijan*

**Background:** For the last years the discussion and researches about efficiency and sequence of use of antiestrogens and aromatase inhibitors in the treatment of advanced breast cancer have not been stopping. For many years antiestrogens (Tamoxifene and Toremifene) were considered standard medicines of first line in the treatment of postmenopausal women with advanced breast cancer. Last years results of researches which have demonstrated advantages aromatasa inhibitor Letrozol over Tamoxifene as first line therapy at the patients with advanced breast cancer were published. At the same time did not investigate comparative efficiency high doses of Toremifene and Letrozole. The aim of this trial is comparative study of Toremifene and Letrozole efficiency in the treatment of patients with advanced breast cancer.
**Material and methods:** 451 receptor statuses not considered patients with advanced breast cancer were involved in this clinical trial. Patient were divided on 4 groups/Hormonal therapy with Tamoxifene at a dose of 20 mg once daily was administered in 117 patients – group I, hormonal therapy with Toremifene at a dose of 60 mg once daily was administered in 115 patients – group II, 106 patients (group III) received Toremifene at a dose of 240 mg daily, 113 patients (group IV) were treated with Letrozole at a dose of 2.5 mg once daily. Patients continued on study medication until disease progression. Efficiency of treatment was determined with following criteria: objective effect, side effects and duration of remission.
**Results:** In the first group 30(25.6%) patients, in second group 38 (33.0%) patients, in the third group 44 (41.5%) patients, in the fourth group 40 (35.4%) had objective effect. Median remission time of 9.2; 11.3; 14.5 and 13.1 months. Side effects in all groups were not significant, did not require specific correction and delay of the treatment.
**Conclusions:** Our data indicated about advantages of Toremifene compared to Tamoxifene and comparable efficiency compared to Letrozole. On the base of the data we can recommend Toremifene for wide use as first line hormone therapy of patients with advanced breast cancer.

**435** PUBLICATION

**Comparison of epirubicin and vinorelbine with cyclophosphamide, epirubicin, and fluorouracil as neoadjuvant chemotherapy for operable breast cancer**

S. Han, K. Kwak, J. Kim, J. Kim, K. Park. *Inje University Sanggye Paik Hospital, Breast Cancer Center, Seoul, Korea*

Reasonable activity and favorable safety of vinorelbine in metastatic breast cancer prompt the integration of these agents into the adjuvant setting. We performed this study to validate the use of vinorelbine as a neoadjuvant therapy in operable breast cancer. The response rates and toxicity profiles of epirubicin plus vinorelbine (EN) were compared with cyclophosphamide, epirubicin, and fluorouracil (CEF) neoadjuvant chemotherapy for operable breast cancer. Eligible criteria for the study was T2 and T3 histologically proven invasive breast cancer without prior systemic treatment and systemic metastasis.
Forty-six patients underwent 4 cycles of EN (epirubicin 75 mg/m$^2$, vinorelbine 30 mg/m$^2$) every 3 weeks and 38 patients underwent 4 cycles of CEF (cyclophosphamide 600 mg/m$^2$, epirubicin 75 mg/m$^2$, fluorouracil 600 mg/m$^2$) every 3 weeks. All the patients underwent curative surgery 3 weeks after the completion of 4 cycles of neoadjuvant chemotherapy. Response rates, which were evaluated by pathologic examination after curative surgery, and adverse effects were analyzed at the admission for operation. Median age and tumor size were well matched between 2 groups (median age: EN 42 yr; CEF 45 yr, median size: EN 5 cm; CEF 5 cm). Response rate was 63% (CR: 4, PR: 25) in EN arm and 60% (CR: 3, PR: 20) in CEF arm after the completion of 4 cycles of neoadjuvant chemotherapy. There was no case of progressive disease during chemotherapy in both arms. Febrile neutropenia was observed in 20% of EN arm and 13% of CEF arm. Grade 3/4 granulocytopenia was observed in 46% in EN arm and 40% in CEF arm during the total of 184 cycles of EN arm and 152 cycles of CEF arm. Breast conserving surgery was performed in 40% of EN arm and 45% of CEF arm.
There was no significant difference in other toxicity profiles during neoadjuvant chemotherapy such as anemia, thrombocytopenia, and oral stomatitis. In summary, vinorelbine was an effective therapeutic agent with reasonable profiles in the neoadjuvant treatment of operable breast cancer. Results of the current study seem to mandate the prospect clinical trial which integrates vinorelbine in the adjuvant setting.

**436** PUBLICATION

**Results of cryosurgery in the treatment of patients with breast carcinoma**

O. Litvinenko, S. Lyalkin, G. Lavrik. *Research Institute of Oncology, General Oncology, Kiev, Ukraine*

Experimental studies have demonstrated the usefulness of cryosurgery for the breast cancer treatment. The aim of our study was to assess the efficacy of preoperative cryosurgery in patients with stage II-III breast carcinoma.
**Materials and methods:** From July 2000 eighty patients with stage II-III breast cancer (mean age 56.7 years) underwent operation, which consisted of preoperative cryotherapy with subsequent modified radical mastectomy (or organ-conserving surgery when appropriate). Control group consisted of 76 patients similar by the main prognostic features, who received conventional treatment. The temperature of the cryoprobe was decreased to minus 190ºCelcius, duration of freezing was 10 minutes. The process of cryosurgery was monitored by intraoperative ultrasonography.
**Results:** We observed no postoperative complications which could be attributed to cryosurgery. To the present date (range of follow-up is from 12 to 58 months) one local relapse (1.3%) was registered in the cryotherapy group, in control group 7 patients (9.2%) developed locoregional recurrence. Three-year overall survival in cryosurgery group was 85.7%, in control – 65.0% ($p > 0.05$), 3-year relapse-free survival was 84.1% in the cryotherapy group, 60.5% in control ($p < 0.05$).
**Conclusions:** Cryosurgery is safe and effective treatment option in patients with stage II-III breast cancer, allows to improve remote results and requires further clinical investigation.

**438** PUBLICATION

**A pilot study of weekly versus 3-week docetaxel in combination with capecitabine in patients with anthracycline-pretreated metastatic breast cancer (CHN-TAX 614)**

Z. Jiang[1], S. Zhang[1], S. Song[1], J. Ren[2], S. Jiao[3], D. Liu[4], Q. Sun[5], H. Wang[6], X. Xie[7], J. Liu[8]. *[1]307 Hospital Affiliated Academy of Military Medica, Cancer center, Beijing, China; [2]Affiliated Cancer Hospital of Peking University, Beijing, China; [3]General Hospital of People's Lineation Army, Cancer Department, Beijing, China; [4]Peking Army General Hospital Hospital, Beijing, China; [5]Peking Union Medical College Hospital, Breast Cancer Department, Beijing, China; [6]Affiliated Cancer Hospital, Tianjin Medical University, Tainjin, China; [7]Shenyang Army General Hospital Hospital, Shenyang, China; [8]Affiliated Hospital, Dalian Medical University, Dalian, China*

**Purpose:** Capecitabine in combination with docetaxel given every 3 weeks has shown a high degree of activity in anthracycline-pretreated metastatic breast cancer (MBC), but with high toxicities. To improve the therapeutic

index, we performed a clinical pilot trial to evaluate the efficacy and safety of weekly or 3-week docetaxel in combination with capecitabine given for 14 days every 21 days.
**Patients and methods:** Patients with at least one measurable lesion were randomized to receive the treatment arms: docetaxel 75 mg/m$^2$ on days 1, oral capecitabine 950 mg/m$^2$ twice daily on days 1–14 (Arm A); docetaxel 37.5 mg/m$^2$ on days 1 and 8, oral capecitabine 950 mg/m$^2$ twice daily on days 1–14 (arm B). Each cycle was repeated every 3 weeks. Patients remained on study for a maximum 6 cycles or until tumor progression or unacceptable toxicity occurred, response assessments were scheduled every two cycles.
**Results:** 64 pts were enrolled, 62 eligible for safety and tumor assessment. Key baseline variables were well balanced. Dominant site of disease was visceral in 66.1%; 24.2% had $\geqslant 3$ organ sites of disease; all patients had previously received anthracyclines, 24.2% for MBC. 43. 6% were ER negative and 46.8% were HER-2 overexpress. The overall clinical response rate of all groups was 59.7% (37/62). There was no progressive disease (PD) after two cycles. Efficacy outcomes were similar in the two arms. The response rate of group A and B were 60%(18/30) and 59.4%(19/32) respectively. There were no drug-related deaths observed. Neutropenia was the most common toxicity. In all, the frequence of Grade 3/4 neutropenia were similar in two arm, but Grade 4 neutropenia of Group A 66.7% (20/30) was higher than Group B 34.4%(11/32), $P = 0.021$.
**Conclusion:** The study confirmed the superior activity of docetaxe-capecitabine combination therapy in anthracycline resistant MBC, and comparing with 3-week schedule, weekly docetaxel plus capecitabine has same high efficacy with a favourable safety profile.

**439** PUBLICATION

**Predictive value of HER-2 status in advanced breast cancer for the response to CMF chemotherapy**

Z. Neskovic-Konstantinovic, S. Susnjar, N. Todorovic-Rakovic, D. Jovanovic, D. Nikolic-Vukosavljevic. *Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

**Background:** HER2 positive breast carcinomas are thought to be more aggressive than HER2 negative once. However, the potential role of HER-2 expression in the prediction of response of to chemotherapy is not yet well established, especially in metastatic breast cancer (MBC) patients. Therefore, the response rate to CMF chemotherapy was assessed in the group of MBC patients, screened for the randomization into the clinical study of CMF chemotherapy combined with a biological agent.
**Material and methods:** HER2 status was determined, using immuni-histochemical method, in paraffin embedded tissue of 99 primaries. In a whole group, 33% were HER 3+. Excluding those pts who entered the clinical study, remaining 39 were treated with CMF chemotherapy alone, irrespective of HER2 status. In this group, pts were almost all postmenopausal, due to previous adjuvant therapy, aged 31–74 (median 54) and had the liver and/or lung involvement in 30/37 cases. ER and/or PR status was positive in 28/39 pts, and inversely correlated with HER-2 status.
**Results:** The overall response rate to CMF was 54%, including 2 (5%) complete remissions. Disease stabilization longer than 6 months was noted in 5 (13%) pts, thus clinical benefit (CB) rate was 67%. The response was not influenced by steroid receptor status, but was significantly influenced by HER2 status: objective response was obtained in 18/26 (69%) HER-2 0–2+, and in only 3/13 (23%) HER-2 3+ tumors. CB was obtained in 20/26 (76%) HER-2 0–2+, and in 6/7 (46%) HER-2 3+ tumors, respectively.
**Conclusion:** Our results confirmed the lower response rate to CMF chemotherapy in HER-2 positive MBC patients, in comparison to HER-2 negative ones. However, it is shown that CMF regimen is still active in selected HER-2 positive BC patients. It seems reasonable to investigate whether the addition of HER-2 inhibitors probably could enhance its efficacy.

**440** PUBLICATION

**Capecitabine (x) in elderly patients with metastatic breast cancer**

P. Zamora[1], M. Álvarez de Mon[2], L. Calvo[3], C. Jara[4], J.A. Virizuela[5], A. Yubero[6], J.I. Chacón[7], J. Mira[8], M. González-Barón[1]. [1]*Hospital La Paz, Servicio de Oncología Médica, Madrid, Spain;* [2]*Hospital Universitario Príncipe de Asturias, Servicio de Oncología Médica, Alcalá de Henares, Spain;* [3]*Hospital Juan Canalejo, Servicio de Oncología Médica, A Coruña, Spain;* [4]*Fundación Hospital de Alcorcón, Servicio de Oncología Médica, Madrid, Spain;* [5]*Hospital Virgen de la Macarena, Servicio de Oncología Médica, Sevilla, Spain;* [6]*Hospital Obispo Polanco, Servicio de Oncología Médica, Teruel, Spain;* [7]*Hospital Virgen de la Salud, Servicio de Oncología Médica, Toledo, Spain;* [8]*H. C. R. Noroeste de Murcia, Servicio de Oncología Médica, Murcia, Spain*

**Background:** Capecitabine is a selective tumour-activated fluoropyrimidine with a demonstrated activity in a wide range of solid tumours. The benefits of oral chemotherapy has changed the daily routine of cancer patients and let them to maintain their normal way of life. The objective of this study is to evaluate the toxicity profile, response rate, overall survival and time to progression in elderly patients with mestastatic breast cancer.
**Patients and Methods:** Patients histologically confirmed of breast adeno-carcinoma, metastatic disease, measurable disease according to RECIST criteria, ECOG PS $\leqslant 2$, age $\geqslant 70$ years, adequate bone marrow, renal and hepatic function were included. Prior chemotherapy, hormonotherapy or radiotherapy for the metastatic disease was allowed. Patients received X monotherapy 1250 mg/m$^2$ b.i.d. (X = 950 mg/m$^2$ in patients with creatinine clearance 30–50 ml/min), days 1–14 every 3 weeks for a maximum of 9 cycles.
**Results:** Twenty three patients were enrolled since July 2002 until June 2004. Median age was 77 years old; ECOG PS 0 in 33.3% and 1 in 66.7% of patients; Tumour histology was adenocarcinoma in all patients. Surgery was performed in all patients. Adjuvant chemotherapy and hormonotherapy was administered in 65% and 74% of patients, respectively. Primary tumour sites were left breast (n = 13), right breast (n = 9) and both (n = 1). Median number of metastatic lesions was 3 (90% with $\geqslant 2$ sites) in bone (57%), lung (43%), liver (43%) and nodes (38%), mainly. A total of 117 cycles (median 4, range 1–9) were administered. Median relative dose intensity was 86% and 100% for X = 1250 mg/m$^2$ and X = 950 mg/m$^2$, respectively. Toxicity: All patients were evaluable for toxicity. Main toxicities are shown in the attached table.

| Toxicity per patient | Grade 1–2 (%) | Grade 3–4 (%) |
|---|---|---|
| Anaemia | 39 | |
| Neutropenia | 26 | 4 |
| Thrombocytopenia | 4 | 4 |
| Hand–foot syndrome | 35 | 13 |
| Asthenia | 39 | 13 |
| Mucositis | 17 | 9 |
| Diarrhoea | 13 | 9 |
| Nausea | 35 | 4 |
| Vomiting | 9 | 4 |

Efficacy analysis: clinical response was evaluated every 3 cycles. Over 16 evaluable patients for efficacy, 2 achieved partial response, 7 stable disease and 7 progressed, resulting in an ORR of 13% (95%CI: 0–29). Median follow up time was 11.5 months, median time to progression was 7.5 months (95%CI: 4.5–10.5) and median overall survival 13.3 months (95%CI: 9.6–16.9).
**Conclusion:** Oral Capecitabine is a well-tolerated chemotherapy treatment in elderly patients with metastatic breast cancer.

**441** PUBLICATION

**Clinical and molecular characteristics of breast cancer patients with brain metastasis: a retrospective study**

S. Dawood[1], T. Bismar[2], T. Alcindor[3], T. Muanza[4]. [1]*Montreal General Hospital, Oncology, Montreal, Quebec, Canada;* [2]*Jewish General Hospital, Oncology, Montreal, Quebec, Canada;* [3]*Mcgill University, Oncology, Montreal, Quebec, Canada*

**Background:** Brain metastasis continues to be a problem amongst patients with metastatic breast cancer despite improved control of systemic disease with new agents. The current analysis was conducted to identify common clinical and molecular characteristics amongst patients suffering from metastatic breast cancer with brain metastasis.