and good tolerability. Preclinical and clinical data show that withdrawal of VEGFR inhibitors may be associated with a rapid tumor growth. We therefore conducted a retrospective analysis in patients who had discontinued trial treatment for progression of disease (PD) and who received a new treatment, in order to evaluate time to progression (TTP), progression free survival (PFS) and overall survival (OS) to the subsequent therapy.
Patients and Methods: Of the 46 patients enrolled in the phase II trial, 44 discontinued trial treatment: 41 for PD, 1 for an adverse event and 2 for personal decision. Two patients are still receiving trial treatment. Thirty-nine patients received a new therapy after progression: chemotherapy and hormonotherapy in 23 (59%) and 9 (23%) respectively, 3 (8%) received both and 4 (10%) were not evaluable. One patient had a rapid progression of disease and died and one was lost to follow up.
Results: Thirty of the 35 (85.7%) evaluable patients had a PD. Median TTP was 106 days, as compared to 229 days after treatment with bevacizumab. PFS at 6 months was 31% (95% CI: 16−46). Sixteen patients died with a median survival of 323 days, and a 6 months OS of 85% (95% CI: 67−93). We evaluated the correlation between serum PDGF-RB, Ve-CAD and circulating endothelial cells, measured at PD after bevacizumab, with TTP and OS: patients with levels of these markers lower than the median value achieved a significantly better TTP and OS with the subsequent treatment.
Conclusions: Though the mechanisms of resistance to bevacizumab are not well defined it is possible that resistance to bevacizumab results in relative resistance to subsequent therapies. Alternatively, rebound increases in VEGF on discontinuation of bevacizumab could result in a more aggressive disease. Much remains to be learned about biologic agents, in particular new trials need to establish whether these therapies should be continued at PD.

5095 POSTER

Elevated circulating estradiol levels are associated with a less aggressive tumour phenotype in postmenopausal breast cancer patients

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Background: It is difficult to correlate circulating hormone levels in premenopausal breast cancer patients with the biology of the tumors, due to physiological fluctuations in menstruating women. This difficulty is overcome in postmenopausal patients, since in them sex hormone levels tend to be constant over time.
Materials and Methods: Circulating hormone levels were measured in 161 previously untreated postmenopausal breast cancer patients within 72 hours of their planned surgery. The obtained hormone levels were correlated with tumor size, histological and nuclear grade, axillary nodal status, DNA-ploidy and Ki67-, c-erb-B2-, p53, Bax-, VEGF- and Nup88-expression.
Results: The only statistically significant correlations found between circulating hormone levels and all tested variables were an inverse one between estradiol and the expression of the apoptosis-associated *Bax* gene ($p = 0.009$), and again an inverse correlation between estradiol and the expression of c-erb-B2 ($p = 0.04$). When comparing hormone levels with each other, a significant correlation between estradiol and progesterone ($p < 0.0001$), an inverse one between estradiol and FSH ($p = 0.04$) and a direct one between LH and prolactin ($p = 0.001$) were found.
Conclusion: Although higher circulating estradiol levels have been repeatedly correlated with an elevated incidence of breast cancer, it appears that in postmenopausal breast cancer patients the tumors thus induced show a biologically less aggressive phenotype.

5096 POSTER

The discordance between hormonal receptor status and c-erb b2 in primary and metastatic breast cancer

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Background: Metastatic breast cancer is one of the most common cause of death from cancer in women. the choice of the best treatment for breast cancer depends on several factors including the patient's age, performance status, menopausal status, as well as tumor size, tumor grade, lymph node involvement, hormonal receptor status, and c-erb b2 status.
The aim of this study was to determine the discordance between hormonal receptor status and c-erbb2 status in primary and metastatic breast cancer.
Materials and Methods: 38 patients with primary breast cancer who developed metastases on follow-up were enrolled into the study. the estrogen receptor (er), progesterone receptor (pr) and c-erb b2 status of the metastases were determined immunohistochemically and compared with the primary breast cancer. Positive hormone receptor status was defined as >5% immunohistochemical staining of tumor cells. c-erbb2 positivity was defined by cytoplasmic membrane staining of 2+ or 3+ intensity. 2+ intensity was assessed by fish or sish techniques.
Results: Variation of er status between primary and metastatic breast cancer was determined in 12 of the 38 (31%) patients and, variation of pr status was shown in 18 of the 38 (47%) patients. 6 cerb b2 negative primary breast cancer became immunohistochemical 3+ in metastatic cancer during follow up.
Conclusions: c erb b2 status is important in the management of metastatic breast cancer. the biological behaviour of primary breast cancer can vary in its metastases. in these metastases, a repeat biopsy may show the new features of the tumor. c erb b2-positive patients should be treated with trastuzumab-based therapy if no contraindications.

5097 POSTER

Poor response to systemic chemotherapy in metaplastic carcinoma of breast

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Background: Metaplastic carcinoma of the breast cancer (MCB) is a rare subtype of breast cancer, for which only anecdotal reports are available regarding its response to systemic chemotherapy.
Aim: To characterize chemotherapy response of MCB patients in a retrospective single-institute study.
Method: We retrospectively reviewed the records of the MCB patients diagnosed at National Taiwan University Hospital (NTUH) between Jan. 1988 and Aug. 2008. The patient-tumor characteristics, treatment modalities, treatment effect, and survival were studied.
Results: 39 MCB patients were identified from 7352 breast tumor patients undergoing biopsy or operation at NTUH. Initial bulky disease (T3−4) was found in 23 patients (56.4%). Expression of estrogen receptor and progesterone receptor were 10.2% and 20.5%, respectively. Nine patients (23.1%) underwent neoadjuvant chemotherapybefore surgery. The regimens included cyclophosphamide/epirubicin/fluorouracil, paclitaxel/cisplatin, vinorelbine/fluorouracil/leucovorin, capecitabine, docetaxel/capecitabine/cisplatin, and docetaxel/epirubicin/cyclophosphamide. Eight of them (89%) experienced disease progression. The response in one patient was not evaluable. Twelve MCB patients (30.8%) developed metastatic disease as initial presentation or during follow-up after primary treatment. Among them, 10 patients received chemotherapy. Only 2 patients (20%) had partial response, all the other 8 patients (80%) had progressive disease. All of the patients with metastatic diseases died of their diseases (3 year survival = 0%). The median survival after metastasis was only 11.3 months (range: 2.73−34.9 months).
Conclusion: MCB had poor response to systemic chemotherapy, either in neoadjuvant setting for locally advanced disease or in salvage setting for metastatic disease.
Key words: Metaplastic carcinoma, neoadjuvant chemotherapy, salvage chemotherapy

5098 POSTER

Clinical outcomes and breast cancer subtypes in patients with brain metastases

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Background: Breast cancer is the second most common cause of brain metastasis. The aim of this study was to investigate clinical outcome by breast cancer subtypes in patients with brain metastases.
Materials and Methods: The authors retrospectively evaluated clinical data from 66 patients who had been diagnosed with breast cancer and brain metastasis between 2000 and 2009. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth receptor-2 (HER2) statuses were tested by immunohistochemical staining. Four survival time intervals were compared according to the subtype (luminal, HER2+, triple negative (TN)): initial diagnosis to distant metastases, distant metastasis to brain metastasis, brain metastasis to death, and overall diagnosis to death.

Results: Twenty (30.3%) of 66 patients were luminal, 20 (30.3%) were HER2+, and 26 (39.4%) were TN. Time interval from initial diagnosis to distant metastases of luminal, HER2+, and TN were 30.0, 17.0, and 17.9 months, respectively ($p = 0.040$). Median time interval from distant metastasis to brain metastasis were 20.6, 19.5, and 9.0 months, respectively ($p = 0.012$). Overall survival from diagnosis to death were 52.9, 33.6, and 25.5 months, respectively ($p = 0.026$). However, Time from brain metastasis to death was not significantly different ($p = 0.276$).
Conclusions: Patients with TN disease were more likely to develop distant metastasis earlier, and poor overall survival. Triple receptor status may be used as a prognostic marker for the breast cancer patients with brain metastasis.

5099 POSTER

Brain metastasis in advanced breast cancer: high risk in HER2 positive but not in triple negative patients

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Background: Central nervous system (CNS) metastasis occurs in about 20% of women with disseminated breast cancer. Triple negative (TN) patients (estrogen receptor (ER), progesteron receptor (PR), and HER2 negative) have a poor prognosis compared to the general breast cancer population, with an increased risk of recurrence, distant metastasis, and death. Also patients with HER2 pos tumors are known to have aggressive disease and several studies has reported a high incidence of cerebral metastasis among this group of patients. Our aim was to evaluate the incidence, pattern and timing of cerebral metastases among patients with advanced breast cancer and compare HER-2 pos patients with HER-2 neg patients including the TN patients.
Material and Methods: Two patient cohorts were examined. The first group consisted of 32 HER-2 pos patients diagnosed with advanced breast cancer and measurable disease, who entered a phase 2 study with 1. line Trastuzumab and weekly paclitaxel. Patients were included between Nov 2001 and Oct 2005. None of these patients had received adjuvant Herceptin. The second group consisted of 59 patients included within the same time period, with normal HER2 status and diagnosed with advanced breast cancer with the same inclusion criteria as above, except they were HER2 neg. (40 ER pos patients and 19 TN patients). They were randomized between first line docetaxel or docetaxel and gemcitabin in a 3 weekly schedule.
Results: All patients have now been followed to death. Eighteen of the 32 HER2 pos patients were diagnosed with cerebral metastases (0.56), compared to 12 patients in the ERpos group (0.30) and only 3 in the TN group (0.16). Median time to cerebral metastases from inclusion was 0.8 years (range 0.5−2.7) for HER2 pos patients. The brain metastases were seen earlier among patients with HER2 over-expression than among HER2 negative patients, though not significant.
Conclusion: Our study shows that HER2 over-expression increases the risk of cerebral metastases significantly as compared to patients without HER2 over-expression. TN patients although having poor prognosis, does not seam to have a high risk of brain metastases. Since more than half of the HER2 pos patients developed brain-metastases, close surveillance (clinical and/or imaging) seams necessary even during effective systemic treatment.

5100 POSTER

Survival of breast cancer patients with brain metastases

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Study objective:
- To study survival of breast cancer patients with brain metastases.
- To study predictive value of tumor size, lymph node involvement and hormone receptor status on the occurrence of brain metastases and survival of patients with breast cancer.

Materials and Methods: 805 patients were diagnosed with breast cancer between Jan. 2000 till June 2008 and registered in Oncology Department in Tripoli Medical Center. 44 (5.5%) patients were included in this study that developed brain metastases diagnosed by CAT scan or brain MRI.
Results: Mean age of these patients were 43.6 years. 72.7% were premenopausal. These patients had large tumor size on diagnosis T3+T4 76.7%. 81.5% were node positive. 72.7% were stage III and IV. 72.7% has negative hormone receptor status. (6/44) 37.5% had isolated brain metastases on presentation. (38/44) 86.4%had recurrence at median duration of 16.5 months. (26/38) 68.4% had brain metastases, out of these (14/26) 53.8% had only brain metastases and (12/26) 46% had brain and soft tissue or bone metastases. (12/38) 31.5% had only visceral metastases as first site of recurrence. (14/44) 31.8% presented as second relapse, with only brain metastases in (10/14) 71.4% and (2/14) 14.3% with brain and soft tissue as liver and lung. All patients received cranial radiotherapy to metastases.
Median duration of survival from first recurrence was 5.8 months. Median duration of follow up was 24.5 months. 25% (11/44) are alive.
Conclusion: Patients with brain metastases are premenopausal and have large tumor size, more node positive, and negative estrogen receptor status.

5101 POSTER

Demographic clinical and pathologic features of breast cancer in males

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Introduction: Male breast cancer comprises 1% of breast cancer cases. The incidence is approximately 1/100.000 per year. Due to the rarity of the disease, the treatment choices are based on the female breast cancer data.
Aim: The study of demographic, clinical and histological characteristics of men with breast cancer that have been monitored, during the last decade, in our department.
Patients and Methods: Patient characteristics were extracted from their medical records and the breast cancer data bank of our department. The registered data concerned age, initial presentation, medical and family history, the histological features of the neoplasms and the TNM staging.
Results: Seventeen men with breast cancer were examined, with median age at diagnosis 65 years (53−79 years old). The initial presentation was a palpable lump in 7 patients, a retraction of the nipple in 3 patients, nipple discharge in 2 patients, scaling of the skin in 2 patients, sub-nipple lump in 2 and lumbar pain in one patient. According to the medical history information, 7 patients were smokers, one did alcohol abuse, 3 were overweight and 8 suffered from hypertension. Positive medical history for familiar or hereditary breast cancer had 3 (17.6%) patients. All tumours were ductal invasive carcinomas, nine of which (53%) exhibited moderate differentiation grade II and the rest, 8 (47%) low differentiation, grade III. Moreover, based on immunohistochemical analysis, 8 cases (47%) were triple negative ER(−) PR(−) HER-2(−), 7 (41%) were ER(+) PR(+) HER-2(−) and 2 (12%) ER(+) PR(−) HER-2(−). The stage of the disease in 7 cases (41%) was IIA, in 3 cases (18%) IIIA, in 3 (18%) IIIB, in 2 (12%) IV, in 1 (5.5%) IIB and in 1 case (5.5%) was stage I. The patients were treated accordingly with anthracyclines and taxanes based chemotherapy, radiotherapy and hormonal therapy (tamoxifen – aromatase inhibitors).
Conclusion: The study indicates that the male breast cancer cases were all HER-2 negative. All tumours were ductal invasive carcinomas and 47% were poorly differentiated. Most patients (53%) were positive for the expression of hormonal receptors while a relatively large percentage (47%) was triple negative.

5102 POSTER

Breast cancer brain metastases – significant differences in biological markers in early vs. late relapse

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Background: HER2 over-expression, negative steroid receptor status, and recently, triple negative status are recognized as factors contributing to the higher incidence of brain metastases (BM). It is also known that BM develops more frequently in young patients. However, it is not known whether these characteristics are the same in the primary breast cancer (BC) that develops early vs. late BM.
Materials and Methods: During 1 year period, 61 patients with BC BM were identified. Median time to BM is 24 months (0–252 months), and median time to BM after other metastatic sites is 24 months (0–252).
Pts were than divided in 2 subgroups: early BM relapse (BM < 5 yrs after BC) and late BM relapse (no relapse at all within 5 yrs and BM $\geqslant$ 5 yrs after BC).
Biological markers were analyzed only on the primary BC specimens.
Results: Results are presented in the table.
There is highly statistically significant difference regarding biological markers of primary BC: negative steroid receptors, HER2 over-expression, and triple negative status are more often in the early BM relapse vs. late BM relapse group ($p < 0.001$; $p = 0.032$; $p \& = 0.029$)