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

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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

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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

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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.

Method: A retrospective review of patients with metastatic breast cancer treated with whole cranial radiation therapy between 1995 to 2005 was conducted. Clinical data was extracted from file review. Pathological specimens were stained for a range of biomarkers.
Results: Data from 117 patients were analyzed. At this time clinical and limited pathological data was available for analysis. The median age of patients at primary diagnosis that would eventually develop brain metastasis was 52 yrs (ranging from 35–75 yrs). Data on initial stage of disease was available for 77 patients of whom 19% presented with upfront stage IV disease, 19% with stage III, 51% with stage II and 11% with stage I disease. Pathological data on primary tumor was available for 63 patients of whom 5% presented with invasive lobular carcinoma and 95% presented with invasive ductal carcinoma the majority of which was grade 3 disease. Estrogen receptor status was available for 95 patients (42% ER+, 58% ER−). Progesterone receptor status was available for 90 patients (33% PR+, 67% PR−). Her2/neu over expression was tested in 51 patients (57% positive, 43% negative). 43 patients had data available for all three receptors (12% ER+, PR+, Her-2/neu−, 27% were negative for all three, 2% ER−, PR+, Her-2/neu+, 33% negative for ER, PR but positive for Her-2/neu, 19% positive for all three, 5% were ER+, PR−, Her-2/neu+ and 2% were ER+, PR−, Her-2/neu−). Sites of first relapse from primary diagnosis included chest wall (14%), lung (28%), bone (28%), liver (15%), and brain (15%).
Conclusion: Based on the limited data available at the time of this analysis breast cancer patients with brain metastasis share common characteristics including high grade primary breast tumors, initial stage II disease, bone and lungs as initial relapse sites, overexpression of Her-2/neu and negative staining for estrogen and progesterone receptors. At present time no reliable biomarker or gene model is available to predict patients at highest risk of developing brain metastasis. This study highlights the significance of developing such a predictive model.

442 PUBLICATION

Radiotherapy for solitary bone metastasis of breast cancer

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Background: The bone metastasis is considered one of the most advanced status of malignant tumor, but life expectancy of patients varies widely according to the tumor origin. Breast cancer patients with bone metastases may survive for comparatively long periods. The purpose of this study is to assess the prognosis of breast cancer patients with solitary bone metastasis after radiotherapy.
Material and methods: The medical records of 121 cases that were irradiated for bone metastases of breast cancer at Kyushu University Hospital from 1989 to 2004 were retrospectively reviewed. Fifteen were found to have solitary bone metastasis based on bone scintigraphy results. All of 15 patients were female and the median age of them was 53 years. They recieved 45 to 60 Gy(median, 50 Gy) in 15 to 30 fractions with radical intent. Chemotherapy was given after radiotherapy in 7(47%) patients. The median follow-up period was 28 months.
Results: The overall survival rates were 78% at 5 years, and disease free survival rates were 49% at 5 years. Irradiated bone metastases showed regrowth only in 3 patients, and the period of regrowth were 9 months, 11 months, and 59 months respectively.
Conclusions: In our results, the patient with solitary bone metastasis of breast cancer is expected to have a good prognosis.

443 PUBLICATION

A novel weekly sliding regimen of docetaxel to treat metastatic breast cancer (MBC) patients with severe hepatic or haematological dysfunction

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Background: Docetaxel is known to be the most effective drug for MBC. The usual 3-weekly dose (100 mg/m^2) is inappropriate for patients with gross liver dysfunction (as the drug is excreted mainly through the liver) and pancytopaenia due to extensive bone marrow infiltration. In this study we describe a weekly sliding scale of docetaxel for treating such patients.
Methodology: The primary objective of this retrospective study was to determine whether a low dose of docetaxel (30–35 mg/m^2), administered initially at weekly intervals (for a maximum of 12 cycles) was effective in normalising compromised haematological/ hepatological parameters in cases of MBC. Following normalisation of these laboratory parameters, dosing was reverted to a 3-weekly schedule (60–75 mg/m^2) for a further 4–6 cycles. MBC patients at Nottingham City Hospital with the above criteria, treated as described, between December 2003 and April 2005, were recruited. Secondary objectives included median time to normalisation so as to permit 3-weekly dosing; overall response; duration of response and toxicities of treatment.
Results: 14 patients (average age 60 years) with altered parameters (11 liver, 2 haematology and 1 both) were recruited. 7/14 (50%) patients received both initial weekly followed by 3-weekly docetaxel and achieved stabilisation of altered parameters. Improvement was achieved with ~5 cycles of weekly low dose docetaxel. A gap of ~19 days was allowed between weekly and 3-weekly schedules. The relative dose intensity (RDI) was 115±8% during the weekly regime (relative to an expected dose of 75 mg/m^2 3-weekly). For those subsequently receiving 3-weekly docetaxel, the RDI for the entire regime was 89±13%. Of the 7 who completed treatment, 1 achieved complete response, 1 stable disease and 2 partial response (RECIST criteria) of 2–3 months duration from the end of treatment. The other 3 had progressive disease at the end of treatment. The 7 patients whose parameters failed to stabilise with weekly docetaxel, progressed further or died during treatment (range 9 days-6 months). The grade 2/3 toxicities encountered during weekly treatment included neutropaenia (28%), diarrhoea (28%), mucositis (28%) and sepsis (21%).
Conclusion: The study demonstrates that this novel weekly docetaxel regime is effective and safe in normalising severe haematological and hepatic dysfunction in MBC and allows standard treatment to follow. A prospective study is warranted for further verification.

444 PUBLICATION

Long-term safety of oral ibandronate for metastatic breast cancer: 4-year treatment data

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Background: Metastatic bone disease is a frequent complication of cancer causing considerable morbidity. Current guidelines for breast cancer patients with bone metastases recommend continuous bisphosphonate use, which may constitute several years of therapy. Oral at-home treatment is more convenient for long-term therapy, and some intravenous bisphosphonates are associated with nephrotoxicity. Here, we report pooled trial data from breast cancer patients treated for 4 years with oral ibandronate, which significantly reduced skeletal complications in Phase III trials.
Methods: During an initial phase, metastatic breast cancer patients were treated for 2 years with placebo or oral ibandronate 50 mg as part of Phase III trials. In a 2-year extension phase, all patients were treated with oral ibandronate 50 mg, but were differentiated according to the treatment received during the initial phase (placebo/50 mg and 50 mg/50 mg groups). Results from the initial (Years 1–2) and extension (Years 3–4) phases were analyzed separately. Safety was assessed by adverse event (AE) reports and laboratory evaluations.
Results: A total of 115 patients were included in the study, with 79/115 (69%) receiving ibandronate for the full 4 years and 36/115 (31%) receiving placebo during the initial 2 years. Most patients experienced at least one AE, with a comparable frequency rated as serious across different groups (initial phase: placebo 44.4%, 50 mg 31.6%; extension: placebo/50 mg 30.6%, 50 mg/50 mg 36.7%). Treatment-related AEs occurred in 19.4% of patients in the placebo group and 35.4% of patients in the 50 mg group in the initial phase, compared to 5.6% (placebo/50 mg) and 6.3% (50 mg/50 mg) in the extension. Five patients experienced treatment-related AEs that were graded severe: three patients during Years 1–2 (50 mg group) and two in Years 3–4 (50 mg/50 mg group). All AEs leading to withdrawal, except for two cases of esophagitis, were considered unrelated to treatment. There were no clinically-relevant laboratory abnormalities and parameters of renal functioning remained normal throughout the study.
Discussion: Once-daily oral ibandronate 50 mg was well tolerated for up to 4 years. The incidence of AEs was similar in patients receiving oral ibandronate for 2 or 4 years. The frequency of treatment-related AEs was low. The efficacy and convenient dosing of oral ibandronate improves the long-term palliative care options for breast cancer patients.