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.