Thursday, 22 March 2012 12:30–13:30

POSTER SESSION

Locally Advanced and Metastatic Disease

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A Review of Clinical Endpoints and Use of Quality of Life Outcomes in Phase III Metastatic Breast Cancer Clinical Trials

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Background: The management of metastatic breast cancer (MBC) is often considered to be palliative, with most interventions intended to relieve disease symptoms, minimize treatment effects and prolong patient survival. The impact of disease and treatment on a patient's functional abilities has led to the emphasis of incorporating quality of life (QoL) measures into clinical trials. The primary objective of this study is to evaluate phase III clinical trials in MBC, and assess the inclusion of QoL as an endpoint, in addition to conventional progression and survival endpoints.

Methods: A structured PubMed search was conducted to identify phase III clinical trials published between Jan. 1990 and Aug. 2011, which evaluated systemic treatment in MBC patients. Data pertaining to treatment regimens, study endpoints and clinical findings were collected, with a particular focus on progression-based (PB), overall survival (OS), and QoL endpoints. The instrument(s) used in evaluating QoL were also noted (when applicable).

Results: Of 520 publications identified, 122 phase III MBC clinical trials met the inclusion criteria. Of these studies, 98.4% and 95.9% included PB and OS respectively, as clinical endpoints, while QoL was assessed in only 46 (37.7%) studies. 14 instruments were identified as QoL measurement tools among these studies, with EORTC QLQ-C30 and FACT-B accounting for 54.7% of the instruments used. While the inclusion of QoL was not associated with the significance of PB results, there was an association between the inclusion of QoL and OS results, with 59% of significant OS studies and 32% of non-significant OS studies including QoL as a clinical endpoint ($p = 0.016$). When stratified by treatment arm, it was found that studies favouring standard therapy were more likely to include QoL (75%, $p = 0.045$), compared to those favouring the intervention (56%), and those without significant differences (32%).

Conclusions: Although the importance of QoL is often emphasized in MBC management and treatment decisions, only one-third of identified phase III clinical trials included an assessment of QoL. About half of these trials showed no statistically significant differences in QoL endpoint; of note, instruments of varying validity were utilized. There needs to be greater emphasis on the evaluation of QoL, with the use of standard and validated QoL tools in MBC clinical trials, especially as we increasingly focus on progression-based endpoints.

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Evaluation of Megasterol Acetate in Locally Advanced and Metastatic Breast Cancer in the era of Aromatase Inhibitors

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Background: There is no cure from metastatic breast cancer and the aim of treatment is to palliate symptoms, delay disease progression & prolong survival [1]. Median overall survival approaches two years, with a range from a few months to many years [2]. Megestrol Acetate (MA) is a progestin which has activity in Tamoxifen refractory, oestrogen receptor (ER) positive breast cancer, but the efficacy of MA following the use the 3rd generation aromatase inhibitors is unknown [3]. We performed a retrospective audit of the efficacy of MA in metastatic & locally advanced breast cancer patients who had progressed following treatment with aromatase inhibitor.

Materials and Methods: Breast cancer patients who had received treatment with MA at the Luton & Dunstable Hospital between 2001 & 2011 were identified from the Oncology Unit patient letter database by searching for the word 'Megace'. Treatment received and clinical outcomes were obtained from the patient notes. Progression free survival was evaluated.

Results: 49 patients were identified with a median age 67 years (range 39–100). All patients had received MA 160 mg daily orally following 3 or more lines of endocrine therapy, which included at least one aromatase inhibitor. 44 (90%) of patients had metastatic disease and 5 (10%) patients had locoregional disease only. All patients had ER positive disease and the HER2 status was: 36 (74%) negative, 3 (6%) positive, 10 (20%) unknown. The tumour pathology was: 35 (71%) Invasive ductal, 13 (27%) invasive lobular, 1 (2%) tubulo-lobular. The median PFS was 12 weeks with a range of 2–110 weeks. Median PFS in patients with 2 or more sites of metastatic disease was 10 weeks (range 2−20 weeks). There was no difference in PFS according to tumor pathology ($p = 0.46$).

Conclusion: Patients with locally advanced or metastatic ER positive breast cancer can obtain clinical benefit from treatment with MA following disease progression with a 3rd generation aromatase inhibitor. No difference was seen in DFS according to tumor pathology, but patient numbers were small. A prospective audit is underway to further evaluate MA in this patient group.

References

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The Prognosis and the Validity of Early Detection of Bone Recurrence After Breast Cancer Surgery

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Background: Intensive routine diagnostic evaluation including bone scans after surgery for breast cancer is not considered appropriate because of less cost-effectiveness. However, bone is the most popular metastatic site, and the patient with bone recurrence alone seems to have better prognosis than the patient with lung or liver metastasis. In the present study, we examined the prognosis of patients with bone reccurrence to clarify the validity of bone examination as a routine Follow-up after breast cancer surgery.

Materials and Methods: Four hundred and sixteen patients who underwent operation for primary breast cancer at Niigata University Hospital during 1999–2008 were entered into the present study. Patients with distant metastasis at surgery were excluded. Almost all the patients entered in the present study have received annual bone scan. The patients records were examined, and the patients with distant recurrences were divided into 3 groups by the first recurrence site; group B included the patients of bone recurrence as the first recurrence site, group BM included both bone and other distant recurrence as first site, and group M included distant recurrences except bone as the first sites. The disease free survival (DFS) and overall survival (OS) were analyzed and compared among these three groups. Statistical analysis was performed by Logrank test, and the statistical significance was defined as $p < 0.05$.

Results: Among 416 patients, distant recurrence was recognaized in 52 patients; 13 patients belonged to group B, 4 patients belonged to group BM and 35 patients belonged to group M. There was no statistical differrence in DFI or OS among the three groups. In group B, despite all 5 patients who finally progressed distant recurences outside bone have died, all 8 patients who showed bone metastases alone have alived. Moreover, DFI was significantly prolonged in these alived 8 patients compared with died 5 patitents in group B ($p < 0.05$). Among alived 8 patients of bone recurrence in group B, 6 patients were asymptomatic, and bone metastases were detected at first with follow-up bone scintigraphy.

Conclusion: Our results suggest that the prognosis bone metastasis alone after breast cancer surgery may present good prognosis in some caces. Because the recent management with anti- cancer drugs such as chemo-, hormonal, molucular-targeting drugs, and bisphosphonates have been progressing, the early detction of bone recurrence seemed to be valid.

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A Phase II Study of Pegylated Liposomal Doxorubicin Combined with Cyclophosphamide / 5-fluorouracil as Second Line Chemotherapy in Patients with Metastatic Breast Cancer Who Failed Previous Taxane-based Treatment

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Background: Although antracycline and taxanes are frequently used in both adjuvant and metastatic setting of breast cancer, treatment