Abstract. Background: We assessed the effect of zoledronic acid on quality of life (QOL) and pain outcome in breast cancer patients with bone metastases using the European Organization for Research and Treatment of Cancer bone metastases module (EORTC QLQ-BM22). Patients and Methods: Three hundred sixty-six breast cancer patients receiving zoledronic acid for bone metastases from 13 Centers were prospectively enrolled. QOL was evaluated using the EORTC QLQ-BM22 and pain outcome were measured monthly with a Visual Analog Scale (VAS) score for 24 months. Results: No significant change of functional scale (functional interference and psychosocial aspects) was reported. Significant reduction of the symptom scale was noted after treatment compared with the baseline. The painful site subscale was significantly reduced during the first 12 months, with the exception the 6-month follow-up of point. Pain characteristics subscale was also significantly lower from the 2-month time point onwards. VAS scores indicated a significant reduction in pain over the course of the study to the 22-month time point follow-up compared to the baseline. Conclusion: Zoledronic acid treatment improved QOL of breast cancer patients with bone metastases by relieving bone pain.

Breast cancer is the most frequently-diagnosed cancer and the leading cause of cancer death in females worldwide (1). Bone is the most common site for metastasis in breast cancer, and patients with advanced breast cancer are at high risk for developing bone metastases and experience skeletal complications (2, 3). Patients with bone metastases often develop moderate to severe pain which significantly decreases functionality and quality of life (QOL) (4, 5). Therefore, delaying the onset and/or reducing pain associated...
with bone metastases is an important goal in the palliative
treatment of patients with bone metastases from breast
cancer.

Zoledronic acid, a bisphosphonate that potently inhibiting
osteoclastic activity, has been shown to significantly reduce
the overall risk of skeletal complications and provide durable
pain reduction in patients with bone metastases from breast
cancer (5-7). Zoledronic acid treatment improves QOL, a
primary goal of treatment in palliative oncology as it
constitutes the international standard for patients with bone
metastases from breast cancer.

Herein, we report the effect of zoledronic acid on QOL
assessed through the use of the European Organization for
Research and Treatment of Cancer Quality of Life
Questionnaire for Patients with Bone Metastases (EORTC
QLQ-BM22) and pain outcome in women with breast cancer
metastatic to bone during the first 24 months of treatment.

Patients and Methods

Patients. This phase IV, single-arm, non-comparative, open label,
and observational study was conducted across 13 medical centers in
Taiwan between July 2008 and November 2012. A total of 366
breast cancer patients with bone metastases who underwent
zoledronic acid treatment according to standard of care under the
supervision of the treating physician were enrolled in this study. As
a standard of care, patients received 4 mg of zoledronic acid via
15-min intravenous infusion every month for up to 24 months.
Inclusion criteria were as follows: female >20 years of age with
histologically or cytologically confirmed diagnosis of breast cancer
and radiological evidence of one or more bone metastases.
Exclusion criteria included radiotherapy to bone within three
months prior to study and prior treatment with bisphosphonates.
Pregnant and lactating females were also excluded. The study was
approved by the Institutional Review Boards or Ethics Committee
for each site and all patients provided written informed consent prior
to enrollment.

Quality of life assessment with EORTC QLQ-BM22. The 22-item
EORTC QLQ-BM22 questionnaire assesses disease symptoms
related to bone metastases. It contains four subscales: painful sites
and pain characteristics on the symptom scale and functional
interference and psychosocial aspects on the functional scale. All
items were scaled from 1 (not at all) to 4 (very much), in which a
higher score indicates greater distress in symptom scales while a
higher score in functional scale indicates greater functional ability.
Each scale was converted to a score ranging from 0 to 100.

Pain assessment. A horizontal Visual Analog Scale (VAS), ranged
from 0 to 100 millimeter (mm), anchored by word descriptors at each
end was used for patients’ self-assessment of pain. The patient marked
on the line the point that they felt represented their perception of their
current state. The VAS score was determined by measuring from the
left hand end of the line to the point that the patient marks.

Statistical analysis. A change of score from baseline of more than
10% as analyzed by longitudinal data with mixed model was
considered clinically significant. All statistical tests were performed
using a two-sided test at the 5% significance level.

Results

Table I lists the baseline characteristics of the 366 patients.
The median time between first breast cancer diagnosis and
bone metastases was 3.7 years. Patients were diagnosed with
bone metastases of a median of 5.4 months before zoledronic
acid treatment.

Table II shows the number of patients which completed
the EORTC QLQ-BM22 questionnaire and the results. The mean
baseline value of the two functional subscales, functional
interference and psychosocial aspects, were 69.2
and 59.7, respectively. No significant change in these two
functional subscales was observed throughout the study
period. Significant reduction of symptom scale, however,
was noted after treatment compared with the baseline. With
the exception of the 6-month follow-up point, painful site
subscale decreased significantly during the first 12 months.
Significantly decreased pain characteristics subscale was also
reported by patients from the 2-month time-point onwards
compared with the baseline.

Bone pain was measured from 0 mm to 100 mm according
to a VAS (Table III). The mean pain VAS score was 35.5 mm
at baseline and decreased significantly over the course of the
study to the 22-month time point follow-up. The reduction
of VAS pain score after the administration of zoledronic acid
was in agreement with the decreased pain characteristics
subscale in the EORTC QLQ-BM22.

Discussion

Breast cancer metastatic to bone results in intractable bone
pain and skeletal morbidities that negatively impact patients’
Zoledronic acid treatment improves the QOL of patients by preventing skeletal complications and providing relief from bone pain, and is the standard-of-care for breast cancer patients with bone metastases (8-10). In a double-blind, randomized, placebo-controlled trial that involved 228 Japanese patients with bone metastases from breast cancer, the zoledronic acid-treated group showed statistically significant improvement in pain scores, which were consistently below baseline, at 4 weeks and at every subsequent time point during the study, when compared to placebo (8).

The present study was designed to determine the effect of zoledronic acid on the QOL of breast cancer patients with bone metastases in the aspect of pain management. QOL is most frequently addressed and measured in clinical trials by use of a core measure questionnaire such as the EORTC QLQ-C30. The present study used the EORTC QLQ-BM22 that was designed to address issues relating to bone metastases (11). The EORTC QLQ-BM22 results showed that despite no improvement of functional scale (functional interference and psychosocial aspects) was reported, significant reduction of symptom scale was observed after treatment compared to baseline. Painful site subscale decreased during the first 12 months and pain characteristics subscale was significantly lower from the 2-month time point onwards compared to baseline.

Results of the 24-month analysis of patient self-assessment of bone pain by using the VAS score indicate that breast cancer patients metastatic to the bone experienced clinically significant levels of pain relief throughout the course of the treatment. This findings is consistent with the findings of symptom scale of the EORTC QLQ-BM22.

A potential limitation to this study design is that pain assessment was subjective and conducted at fixed time points a month apart which may not reflect all experiences of pain associated with the disease. Other limitations of the study included the lack of control arm or placebo. In summary, given the demonstrated bone pain-relieving efficacy of zoledronic acid, this phase IV, prospective, and observational study has confirmed the significant clinical benefits of zoledronic acid in patients with bone metastases secondary to breast cancer with EORTC QLQ-BM22.

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Conflicts of Interest

The Authors have declared that no competing interests exist.

References


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