Survival analysis of patients with metastatic bone disease administered anti-resorptive agents

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Backgrounds Anti-resorptive agents are administered during the overall management of patients with metastatic bone disease to delay and prevent skeletal-related events and other side effects of anti-resorptive agent-related osteonecrosis of the jaw (ARONJ).

Case 1. Anti-resorptive agents started before dental examination.

Periodontitis infection
→21 Extraction
If the patient was to undergo an examination before being administered anti-resorptive agents, would the effects of ARONJ that reduce quality of life be lessened?

The patient was deceased after living with ARONJ for 150 days

Case 2. The patient was deceased soon after pre-treatment dental examination.

Periodontitis infection
→16 46 Extraction
If the patient did not have the teeth removed, would the end of his life have been better?

The patients could not bite on the right side and he passed away 10 days after the extraction.

During life, performing dental treatment and oral care is imperative in patients irrespective of ARONJ.

Objectives This retrospective study is aimed to evaluate the overall survival rates of patients with metastatic bone disease in our hospital.

Participants and Methods

Study Design

This was a single-center, retrospective, observational study.

Participants

Patients who were administered anti-resorptive agents for metastatic bone disease from April 2012 to March 2015 [n=270, M:114, F:156, 63 (26-90)y]

Methods

The Kaplan–Meier analysis and log-rank test were used to estimate survival rates of all participants, including those administered zoledronic acid, or denosumab and those with a primary tumor. Statistical analysis was performed by a statistical software; Stata14 (StataCorp LLC, TX, USA).

Table 1. Anti-resorptive agents

Anti-resorptive agents	n
Zoledronic acid and Replacement of Zoledronic acid with denosumab	110
denosumab	160
Total	270

Zoledronic acid or denosumab administration

Zoledronic acid was administered at a dose of 4 mg every 3 – 6 weeks over 15 minutes by intravenous injection, and denosumab was administered at a dose of 120 mg every 4 – 5 weeks, by subcutaneous injection. Zoledronic acid dose adjustment was carried out based on the patient's calcium level and/or renal function.

Table 2. Characteristics of participants

primary tumor	n
Lung	105
Breast	51
Prostate	15
Kidney	15
Colorectal	13
Liver	12
Uterus	10
Stomach	5
Other	44
Total	270

The Ethics Committee of Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences approved this study (Approval No. ken 1509-021).

Results

The Kaplan–Meier survival estimates and survival rates from starting administered anti-resorptive agents in metastatic bone disease.

1) All participants

Figure 1. The Kaplan–Meier survival estimates of all participants

2) Zoledronic acid or denosumab

Figure 2. The Kaplan–Meier survival estimates of participants given zoledronic acid or denosumab

◆ The overall survival rate of the denosumab group was higher than that of the zoledronic acid group, and Kaplan–Meier survival estimates of both groups were significantly different ($P < 0.01$).

3) Primary tumor

Figure 3. The Kaplan–Meier survival estimates of participants with a primary tumor

◆ The overall survival rate of the breast cancer group was higher than that of the group of other primary tumors, and Kaplan–Meier survival estimates of both groups were significantly different ($P < 0.01$).

Discussions

- Considering the survival rates, treatment plans including the removal of dental infection should be constructed.
- It is necessary to predict long-term prognosis and oral management for breast cancer patients who received denosumab as a treatment in particular, because they have significantly higher survival rates than other patients.

Conclusions

This study revealed that breast cancer patients who received denosumab as a treatment showed longer survival than those with some other type of cancer. Overall, dental treatment and oral care is essential to ensure high survival rates among patients with metastatic bone disease.