

Abstract

Reduced risk of bone metastases in breast cancer patients treated with Cox-2 inhibitors

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Background: Approximately 40–70% of women diagnosed with breast cancer will develop bone metastases. The level of cyclooxygenase-2 (Cox-2) is overexpressed in human bone metastases and correlates with the occurrence of bone metastases in animal models. We hypothesize that the use of Cox-2 inhibitors in early phases of breast cancer could protect against the development of bone metastases. **Methods:** The medical charts of all patients treated for stage II and III breast cancer between 1999–2005 were reviewed. Patients were subsequently subdivided into those who took Cox-2 inhibitors (celecoxib, rofecoxib or valdecoxib) for at least 6 months following the diagnosis of breast cancer and those who did not. The diagnosis of bone metastases required conclusive radiologic imaging. Fisher's exact test and a multivariate logistic regression were used to analyze the data. **Results:** A total of 692 patients were included in this analysis. The patients' mean age was 59 and the mean follow up was 3.9 years. Eleven percent (74/644) of patients who did not take Cox-2 inhibitors developed bone metastasis compared to two percent (1/48) of those who did (Fisher's exact test $p = 0.05$). Significant predictors for developing bone metastases using a multivariate logistic regression model were: 3 or more positive nodes ($p < 0.001$; Odds Ratio = 3.19, 95% CI = 1.79 - 5.70), stage IIb-IIIc ($p = 0.001$; OR = 4.61, 95% CI = 2.19–9.72) and use of Cox-2 inhibitors ($p = 0.025$; OR = 0.10, 95% CI = 0.013–0.75). Adjusting for TNM stage, of the 327 patients in stages IIb-IIIc, 21.5% (63/293) had bone metastasis in the non-Cox-2 group vs. 3% (1/34) in the Cox-2 group ($p = 0.006$). In this high-risk group of patients, the calculated odds ratio for development of bone metastases associated with the use of Cox-2 inhibitors was 0.10 (95% CI = 0.014–0.78). There was no significant difference between the groups in the number of patients that received adjuvant radiotherapy, chemotherapy, or hormone therapy. **Conclusions:** This retrospective study suggests that the use of Cox-2 inhibitors can reduce the risk of bone metastases in patients with stage II and III breast cancer. Prospective randomized trials of adjuvant Cox-2 inhibitors in patients with high-risk breast cancer are needed to validate this conclusion.