

CORRESPONDENCE

Rates of Myocardial Infarction and Coronary Artery Disease and Risk Factors in Patients Treated With Radiation Therapy for Early-stage Breast Cancer

We read the interesting article by Jagsi et al on the increased rates of coronary artery disease in patients treated with radiation therapy for early-stage breast cancer.¹ In their study, those authors concluded that the findings support further assessment of clinical outcomes when newer techniques of chemotherapy planning are employed as well as investigation of the potential role of innovative techniques. However, there was no mention of the novel radiosensitizing and chemosensitizing effects of bisphosphonates (BPs), which inhibit tumor cell adhesion to bone, and tumor growth in breast cancer.

We recently demonstrated that zoledronic acid (ZOL), the third-generation of BPs, increased disease-free survival in pristine-induced plasmacytoma in BALB/c mice.² In another study, we demonstrated that using the combination of ZOL and radiation always synergistically enhanced growth inhibition of breast cancer cells compared with either agent alone.³ The results from the combination of ZOL and radiation are novel and intriguing, because they immediately suggest the clinical utility of using ZOL combined with radiation to avoid serious side effects of radiotherapy, especially in patients with breast cancer.

All of these results raise the possibility that nitrogen-containing BP, ZOL, with its direct antitumor effect and as a radiosensitizing and chemosensitizing agent, may be a valuable adjunct to the treatment of patients with breast cancer. Combining BP treatment with radiation or chemotherapy produces the same effect with a lower radiation dose or lower fraction numbers, thus avoiding serious cardiac side effects of radiotherapy.

REFERENCES

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Reply to Rates of Myocardial Infarction and Coronary Artery Disease and Risk Factors in Patients Treated With Radiation Therapy for Early-stage Breast Cancer

We appreciate Ural and colleagues' comments in response to our article.¹ Our findings support the investigation of novel approaches to minimize cardiac toxicity from the treatment of breast cancer. Novel methods of radiation therapy administration seem to be the most appropriate targets for investigation, because more conformal techniques may permit a lower dose to cardiac structures while maintaining an adequate tumoricidal dose to targeted structures. However, we agree with Ural and colleagues that other innovative approaches also may prove

useful to this end, including the possibility of combining radiation therapy with other agents. Nevertheless, it is important to note that such combination therapy must be proven to provide an enhanced therapeutic ratio compared with standard treatment with radiation alone. We believe that it is extremely premature to speculate that "combining bisphosphonate therapy with radiation...produces the same effect with lower radiation dose...avoiding serious cardiac side effects of radiotherapy." Like with any new approach, the use of bisphosphonates, if supported by preclinical data, must be explored carefully in the clinical setting with Phase I, II, and III studies to determine whether it actually is safe and efficacious to administer these agents in combination with radiation therapy in the setting of adjuvant treatment of breast cancer. Only after long-term follow-up from clinical studies may we determine whether this proposed approach may have any impact in reducing the potential for radiation-related cardiac toxicity while maintaining adequate tumor control.

REFERENCE

1. Jagsi R, Griffith KA, Koelling T, et al. Rates of myocardial infarction and coronary artery disease and risk factors in patients treated with radiation therapy for early-stage breast cancer. *Cancer*. 2007;109:650-657.

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