
Early Breast Cancer Therapy and Cardiovascular Injury

The paper by Jones et al. (1) provides an excellent review of the cardiovascular toxicity incurred during treatment for breast cancer. Late cardiotoxicity from anthracyclines has been recognized in survivors of childhood cancer (2) and is more recently being addressed in survivors of breast cancer. The section by Jones et al. on “Prevention and/or Treatment” contains many important approaches. It is surprising, however, that dexrazoxane is not mentioned.

Dexrazoxane was shown in the 1980s to afford protection from cardiotoxicity in women with breast cancer (3). Its use was limited after a multicenter trial, in advanced breast cancer, reported by Swain et al, confirmed cardioprotection, but showed, in 1 of the 5 study arms, a better tumor response in the control patients compared with those treated with dexrazoxane (4). As a result, the indication for breast cancer was restricted to patients who had already received 300 mg/m2 doxorubicin, pending further trials. Further trials were subsequently conducted in patients with pediatric cancers, including Ewing’s sarcoma, osteosarcoma, Hodgkin’s lymphoma, and leukemia. These trials demonstrated cardioprotection, with no decrease in anticancer efficacy, when dexrazoxane was added to chemotherapeutic protocols. It is therefore used with initial therapy in pediatric patients. It has allowed treatment with cumulative doxorubicin doses up to 600 mg/m2, without cardiac failure (5). It is, therefore, time for the use of dexrazoxane to be investigated again in women with breast cancer during initial treatment, to provide them with protection against future cardiotoxicity.

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We thank Dr. Steinherz for the important comments regarding the use of dexrazoxane as a prevention/treatment strategy for anthracycline-induced cardiotoxicity in cancer patients. The primary focus of our paper was to examine the risk of and preventive/treatment strategies for long-term global cardiovascular disease (CVD) as opposed to the specific entity of anthracycline-induced cardiotoxicity (1). We feel that this is important to stress because the risk of late-occurring CVD in women diagnosed with early breast cancer likely far exceeds the risk of symptomatic anthracycline-induced cardiac dysfunction during therapy. Clearly, prevention/treatment of cardiac toxicity is of major clinical importance in breast and several other cancer populations, as highlighted by Dr. Steinherz. Further, acute and delayed cardiac toxicity likely contribute to the risk of late-occurring CVD as a component of the “multiple-hit” hypothesis as described in our paper (1). To this end, we agree with Dr. Steinherz that clinical trials of dexrazoxane are required in women receiving chemotherapy in the early stages of disease. However, we wanted to highlight strategies for the treatment of risk factors for the global prevention of CVD in women (e.g., lifestyle modification in conjunction with pharmacotherapy) which has not, in our opinion, received adequate attention in oncology.

Finally, to our knowledge, dexrazoxane has only been investigated and approved by the Food and Drug Administration among breast cancer patients in the metastatic (advanced) setting who have received a cumulative dose of 300 mg/m2 (2). Given that the focus of our paper was cardiovascular injury among women diagnosed with early-stage disease, we felt inclusion of this approach was not warranted.

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