Efficacy of Trastuzumab

To the Editor:

We read with interest the article by Adams et al. (1), which describes the efficacy of an yttrium-90-labeled anti-HER2 diabody in a mouse xenograft model of HER2-positive breast cancer. Women with HER2-positive breast cancer have a distinctly worse prognosis than those whose tumors do not overexpress HER2, with an increased rate of relapse, decreased disease-free survival, and increased mortality rate (2). Therefore, therapeutic agents that specifically target HER2 have the potential to significantly impact morbidity and mortality from this devastating disease. Trastuzumab (Herceptin, Genentech, Inc., South San Francisco, CA), approved by the Food and Drug Administration in 1998, is a monoclonal antibody that recognizes the HER2 extracellular domain. Trastuzumab is indicated as a single agent for the treatment of patients with HER2-positive metastatic breast cancer who have received one or more chemotherapy regimens for their metastatic disease, and trastuzumab in combination with paclitaxel is indicated for the treatment of patients with HER2-positive metastatic breast cancer and who have not received chemotherapy for their metastatic disease (3).

Adams et al. state that "although a number of patients treated with trastuzumab have experienced significant antitumor effects, 84% fail to respond" (1). The quoted study (4) enrolled women with HER2-positive metastatic breast cancer whose tumors had progressed after one or two prior chemotherapy regimens. An objective response rate of 15% was seen in the intent-to-treat population, with a response rate of 18% in patients whose tumors strongly overexpressed HER2 (scoring 3+ by immunohistochemistry). In clinical studies of novel oncologic therapies, patients generally respond best when they have not received prior anticancer therapy. A first-line trastuzumab monotherapy study (5) showed an objective response rate of 34% in patients whose tumors showed HER2 gene amplification by fluorescent in situ hybridization. In addition, 14% of these patients experienced prolonged stable disease, for a combined clinical benefit rate of 48%. Indeed, response rate alone may not be the best way to measure the benefit to patients from targeted therapies such as trastuzumab.

We suggest that the overall response rate (34%) and clinical benefit rate (48%) to first-line trastuzumab monotherapy are significantly higher than those stated by Adams et al. (1) and that these are the benchmarks against which the efficacy of newer HER2-targeted agents should be measured in clinical settings.

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References
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