Marti Nelson Cancer Foundation
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Davis, California 95616

February 14, 2011

Re: Comments on FDA Docket No. 2010-N-0621

Dear Dr. Hamburg,

We encourage the FDA to hold a public hearing on its proposal to withdraw approval of the metastatic breast cancer indication for bevacizumab. We believe there are at least two issues of relevance that are best considered or debated at greater length in a public forum.

First, we would like further consideration of an apparent lack of data directly contradicting the results of the E2100 clinical trial, the primary basis for the accelerated approval of bevacizumab for metastatic breast cancer. The results of subsequently published clinical trials testing bevacizumab in combination with other chemotherapeutic agents have certainly been disappointing, and they suggest that bevacizumab is not as valuable a clinical tool for the treatment of breast cancer as many of us had hoped it would be. However, the specific combination of bevacizumab with paclitaxel has clearly been of benefit to some patients with metastatic breast cancer and may offer benefit to many more in the future. We are concerned that fully withdrawing the breast cancer indication at this time will deprive some future patients of meaningful clinical benefit and believe this is an issue worth further public consideration.

We are disappointed that despite substantial resources committed to various bevacizumab clinical studies, Genentech and Roche have not obtained sufficient data to definitively replicate or invalidate the results of the E2100 study of bevacizumab specifically in combination with paclitaxel. However, we do not think this failure alone, at this time, is adequate reason to deny the possibility of clinical benefit from this drug combination to breast cancer patients who cannot afford to obtain it off-label and unreimbursed while we wait for the results of planned clinical trials.

It is clear that many patients treated with bevacizumab may suffer its side effects without receiving benefit, while a minority may receive significant benefit. Unfortunately, no one can predict which patient is which prior to initiating treatment. Ultimately, we believe these difficult regulatory decisions need to be made with the individual patient in mind, both the person who is harmed and the person who is helped. Legal arguments and procedural arguments should take a distant back seat to issues of science, medicine and patient well-being. In the face of substantial uncertainty, each patient, as a valued individual, must make an treatment irreversible decision in consultation with one or more individual physicians. Under these circumstances, more information is always better; thus, our exhortations to the FDA to conduct thorough and even redundant public analysis prior to taking final action and to Genentech and Roche to deploy the necessary resources to answer open and critical clinical questions about bevacizumab as rapidly and unambiguously as possible.

A second issue of broad public health and public policy importance we believe justifies a public hearing is the need to further consider, and more objectively define, clinical significance versus statistical significance in the context of the use of progression free survival versus overall survival as clinical trial endpoints to support drug approval applications. Although such a broad issue would not be the primary purpose of a public hearing, and the issue has been, and will continue to be, debated in other venues, we believe a public hearing on the immediate bevacizumab issue may contribute important understanding to this important technical policy issue.

We believe that a clinically meaningful and statistically significant improvement in progression free survival provides an important clinical benefit to patients, even in the absence of a demonstrated statistically significant improvement in overall survival. Many intelligent and well-informed people disagree with our view on this issue. The bases for agreement and disagreement on this topic are complex and beyond the scope of this letter, but we believe those who disagree with our view would agree that more extensive public discourse on this topic could be valuable.

We understand that the decisions the FDA makes are not easy and are made carefully. We do not have access to all the expertise or data available to the FDA, nor does the public at large, nor does the individual patient or physician in the exam room or hospital room. We believe a public hearing will enhance public understanding of the difficult work performed by the FDA and also provide this specific issue with the careful, complete and public analysis its importance warrants.

Very truly yours,

Robert Erwin
President
Marti Nelson Cancer Foundation