

Collaborating with Stakeholders  
Safety Assurance in Clinical Trials  
Presentation to the FDA  
Thursday, March 23, 2000

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Thank you for coming to the "left coast" and for the opportunity to address you today on issues related to how to leverage Safety Review for New Products and Safety Assurance in Clinical Trials.

I am the Executive Director of Breast Cancer Action, a national education and advocacy organization based in San Francisco. On behalf of our more-than 6000 members, we work to assure that the needs of women with and at risk for breast cancer are appropriately addressed by the various entities that are working in the breast cancer arena. We frequently present testimony to the FDA's Oncologic Drug Advisory Committee on matters related to breast cancer.

My remarks today on clinical trials focus on FDA's approval in September, 1999 of epirubicin, a new breast cancer treatment drug, and on compassionate access to trastuzumab (better known as Herceptin). These two examples point toward steps that can be taken to improve the process of safety review and safety assurance.

Epirubicin was approved by the FDA for treatment for women with early-stage, node-positive disease. The approval was based on data that showed that the drug improves chances of survival when compared to a combination chemotherapy treatment called CMF (cyclophosphamide, methotrexate and fluorouracil). However, women with early stage, node-positive breast cancer are not normally treated with CMF; they are treated with combinations of drugs that include adriamycin. Comparing epirubicin to CMF was not a relevant comparison, and approving the drug based on that comparison did nothing to improve outcomes for women with breast cancer.

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All breast cancer drugs have side effects. In many cases, the long-term side effects are unknown and, because of the need for speedy approval in light of life-threatening nature of breast cancer, will not be known until long after the drugs are approved. Under these circumstances, new breast cancer drugs should not be approved unless they either a) improve overall survival when compared to the currently used treatment, b) improve quality of life for breast cancer patients, or c) significantly reduce the cost of treatment. While safety is and should be the first consideration, it cannot be the only consideration. Breast Cancer Action will actively collaborate with the FDA in the educational aspects of clinical investigations when these criteria are made central to the guidelines under which trials are administered and their results approved.

The Herceptin story reflects these criteria and also highlights the possibilities for collaboration in advancing the interests of all concerned. When Genentech asked Breast Cancer Action to help recruit patients for its Phase III trials, we agreed, provided that the drug be made available on a compassionate basis to women who – based on the biology of their cancer -- might benefit, but who were otherwise ineligible for the trial. While some desperately ill women raised questions about the structure of the compassionate or expanded access program for Herceptin, there is no doubt that the existence of the program both helped women who would otherwise have had no hope, and advanced the completion of the Phase III trial. Herceptin, which actually improves both overall survival and quality of life for some patients, was approved with record speed.

Genentech's willingness to work with the advocacy community to make compassionate access available came after a long and often contentious battle. It is clear now that the model works. The FDA can and should facilitate this kind of collaboration by requiring that a compassionate access program be part of Phase III trials for breast cancer drugs.