January 14, 2011

Margaret Hamburg, M.D.
Commissioner
Food and Drug Administration
Department of Health and Human Services
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dr. Hamburg:

I am writing to urge the FDA to hold a hearing on the use of Avastin in metastatic breast cancer. The Melanoma Research Foundation is the largest and oldest non-profit working exclusively with people affected by melanoma. While this potential hearing is related to breast cancer, the issues around the request for a hearing touch very much on our space.

The last time a drug was approved for metastatic melanoma was over a decade ago, and about 85% of people who take that drug derive no benefit from it. Clearly, the melanoma community is highly interested in a drug development process that moves quickly and effectively to bring investigatory new drugs into the clinical setting. That process is impeded by many factors, and certainly one significant issue is the increasing regulatory burden on drug development. While many aspects of that burden are inescapable, logic dictates that clarity, consistency, and good communication are key components to ensuring that the approval process moves quickly. Having criteria that are unclear or are changed mid-process adds to cost of development and, more significantly, results in delays in ensuring patients have access to drugs that may be life-saving.

The recent situation with Avastin is a case in point, and it raises a number of questions for me and, I suspect, for patients:

Why did the FDA convene an ODAC meeting for the purpose of determining if Avastin should be moved from accelerated approval to full approval in metastatic breast cancer, then use that ODAC as a forum to question if this label for Avastin should be removed altogether?

1411 K Street, NW
Suite 500
Washington, DC 20005

(202) 347-9675
www.melanoma.org

If the FDA had concerns about the efficacy of Avastin in this setting, why didn't they address those concerns with the company and ask for additional data or studies relevant to those concerns?

Why did the FDA ask Genentech for data showing no negative impact on Overall Survival (OS), then critique the use of the drug for, rather, not demonstrating an improvement in OS?

Is OS the only endpoint that is sufficient for full approval of oncology drugs? In the melanoma space we are hearing that Progression Free Survival (PFS) is a satisfactory endpoint, so are the standards different for different tumor types?

If PFS is an acceptable endpoint, then what criteria are used to determine how much PFS benefit is enough? Who makes that decision? Is it patients? Oncologists? Without guidance on this, industry has no concept of what level of efficacy is likely to result in approval.

The actions of the FDA regarding Avastin raise these questions, and more. If for no other reason than that, the requested hearing on this topic should be held.

To be clear, I am not an apologist for industry. In fact, I am often frustrated with the seemingly glacial pace at which industry moves in developing drugs that are potentially relevant to melanoma. To that end, I am very interested in stripping away the excuses that are used to explain this slow pace. When regulators are not clear and consistent, and when dates, data requests, and goals are changed with little notice, industry has the opportunity—legitimately—to point to the FDA as being the barrier to a faster, smoother process.

And these changes have a real impact on patients. Last year the FDA announced that no later than December 25, 2010 they would make a decision regarding approval of a new drug for metastatic melanoma. Less than two months before that date they announced they were postponing the decision until March. The day of that announcement I received a message from a frantic patient. He was battling metastatic melanoma and his doctor recommended this particular drug. The patient was not eligible for the expanded access protocol, or for a clinical trial. He felt, though, that he could hold out until December 25 when, he hoped, the drug would approved. He turned down the opportunity to participate in other trials in anticipation of having access to what he and his doctor considered to be a more promising opportunity. He was shocked to hear about the delay. In his words, "I am not sure I will be alive in March."

I hear from my colleagues working with breast cancer patients that the FDA decision regarding Avastin has had a similar impact on many patients with whom they work. I

am not endorsing regulation by anecdote, but a hearing at which data can be presented clearly and intentionally seems to be warranted in this situation.

Sincerely,

Tim Turnham, PhD
Executive Director
Melanoma Research Foundation

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