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May 22, 2005

Richard Pazdur, M.D., F.A.C.P.
Director
Office of Oncology Drug Products
Center for Drug Evaluation and Research (CDER)
U.S. Food & Drug Administration
5600 Fishers Lane, HFD-150
Rockville, MD, 20857

Dear Dr. Pazdur;

On behalf of the Lung Cancer Alliance (LCA), the only national organization dedicated exclusively to advocacy for lung cancer patients, their families, caregivers, survivors, and those at risk for lung cancer, I am writing to comment on the status of gefitinib, in part based on recent data from the ISEL trial and on the recently closed Southwest Oncology Group (SWOG) clinical trial of gefitinib (Iressa®) for advanced lung cancer which indicated that it would not improve survival.

As the voice of patients with lung cancer, the number one cancer killer, we would like to share with you our concerns in four areas:

- (1.) ***We do not yet know how to fully evaluate the benefits of Iressa®.*** As we shared in the March Oncology Drug Advisory Committee (ODAC) hearing, we understand that the Food and Drug Administration (FDA) is required by statute to evaluate drugs by looking at the safety and efficacy of the data to determine whether the benefits of a drug outweigh the risks. We also understand that molecularly targeted compounds, such as Iressa®, do not always fit neatly into the current evaluation paradigm and patient selection could help to define efficacy based on clinical or biologic features. As we move toward personalized medicine more and more compounds will likely work only for a small subset of patients. We do not yet know how to design clinical trials or evaluate the data from them in these situations or even how to determine who will and won't benefit from these compounds. Iressa® was approved based on strong but not definitive evidence of patient benefit. There are no new safety concerns to warrant withdrawal until the data from all phase IV studies are reviewed.

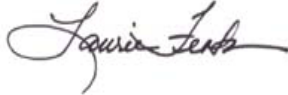
- (2.) ***All of the phase IV Iressa® data is not in yet.*** We also understand that under accelerated approval regulations, some drugs are initially allowed onto the market based on the evaluation of surrogate efficacy endpoints, but are to be fully evaluated after randomized trials of established endpoints, such as survival, are complete. Then the FDA determines if the drug should remain on the market or be removed. We think this evaluation should be done once all of the data is collected, including all phase IV data. Given that the safety profile is more favorable than most standard chemotherapies for lung cancer, Iressa® should not be taken off the market until at least all of the Phase IV data are in.
- (3.) ***Quality of life for advanced lung cancer patients must be considered.*** As you know, the vast majority of lung cancer patients are diagnosed with stage IIIB or stage IV disease. Of the very few therapeutic options available to them most are very toxic and greatly impair their quality of life. While we all agree that survival is a very important end point, we also believe that given our inability to cure this disease, quality of life is an equally important endpoint. Yet, there seems to be no accepted method of evaluation for compounds that improve the quality of a patient's life. Therefore, quality of life never seems to be fully considered. In the case of Iressa, we know some patients are benefiting greatly from Iressa® and it is truly improving their quality of life. Iressa® should not be taken off the market when it is benefiting lung cancer patients with few options.
- (4.) ***A number of biologic selection parameters such as FISH analysis, immunohistochemistry chemistry analysis and mutations analysis were recently presented at ASCO.*** These tests could be prospectively applied to samples from the ISEL trial and the ongoing Iressa versus docetaxel study. If positive, full approval could be warranted in a subset.

Since the March ODAC hearing, many more patients have contacted us to say that they continue to have amazing responses on Iressa® and are terrified of it being taken off the market. It is our understanding that if Iressa® is taken off the market patients who are currently on it will be allowed to continue getting access to the drug as long as they have need for it. While we applaud that decision, we are all still concerned about those patients who try erlotinib (Tarceva®) and have a negative response or a bad reaction. They should be allowed to have the option of trying Iressa®. We know Iressa works for some people and there is no data that shows that if a patient is failed by Tarceva®, they won't respond to Iressa®.

As the representatives of patients with advanced lung cancer we ask that you not act hastily to pull Iressa®--or any other drug that appears to be tolerated--from the market so that doctors and patients can do what they have always done, consider the data and make the decision that is right for them. We know you have regulatory obligations but we also know that those regulations were put in place to help and protect the very patients we are talking about - people with advanced lung cancer. We are telling you we want Iressa® to remain an option.

We at the Lung Cancer Alliance are very interested in speaking with you in person on this issue before any decisions are made on the fate of Iressa®. Please contact me at our Washington, D.C. office, (202) 463-2080. I look forward to speaking with you on this very important issue.

Sincerely,

A handwritten signature in cursive script that reads "Laurie Fenton".

Laurie Fenton
President
The Lung Cancer Alliance

CC: Patty Delaney, Office of Special Health Issues, FDA

CC: Lung Cancer Alliance Board of Directors

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