Summary Minutes of the
Oncologic Drugs Advisory Committee
December 5, 2007
Location: Hilton Washington DC North/Gaithersburg, The Ballrooms
620 Perry Parkway, Gaithersburg, MD

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the December 5, 2007 of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on __January 7, 2008_____.

I certify that I attended the December 5 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____
Nicole Vesely, Pharm.D.
Designated Federal Official, ODAC

_____/s/_____
Maha H. Hussain, M.D.
Committee Chair

Meeting of the Oncologic Drugs Advisory Committee
December 5, 2007

The Oncologic Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 5, 2007 at the Hilton Washington DC North/Gaithersburg, The Ballrooms, 620 Perry Parkway, Gaithersburg, MD. Prior to the meeting, members and invited consultants were provided copies of the background material from the FDA and the sponsor. The meeting was called to order by Maha Hussain, M.D. (Committee Chair); the conflict of interest statement was read into the record by Nicole Vesely, Pharm.D. (Designated Federal Official). There were approximately 250 persons in attendance. There were 2 speakers for the Open Public Hearing session.

Issue: The committee discussed supplemental biologics license application (sBLA) 125085/91, AVASTIN (bevacizumab), Genentech, Inc., proposed indication, in combination with paclitaxel, for the treatment of patients who have not received chemotherapy for their locally recurrent or metastatic, HER2 negative breast cancer.

Attendance:
Oncologic Drug Advisory Committee Members Present (Voting):
S. Gail Eckhardt, M.D., Maha Hussain, M.D. (chair), Michael Link, M.D., Gary Lyman, M.D., Virginia Mason, RN (consumer representative), Joanne Mortimer, M.D.

Special Government Employee Consultants (Voting):
Aman Buzdar, M.D., Ralph D'Agostino, Ph.D., Natalie Portis (Patient Representative)

Non-voting Participants:
Gregory Curt, M.D. (Industry Representative)

Oncologic Drugs Advisory Committee Members Not Present:
David Harrington, Ph.D.
Michael Perry, M.D.
Ronald Richardson, M.D.
Ronald Bukowski, M.D.

FDA Participants (Non-Voting):
Richard Pazdur, M.D., Patricia Keegan, M.D., Lee Pai-Scherf, M.D., Mark Rothmann, Ph.D., Laura Lu Ph.D., Patricia Cortazar, M.D.

Designated Federal Official:
Nicole Vesely, Pharm.D.

Open Public Hearing Speaker:
Robert Erwin, President, Marti Nelson Cancer Foundation
Carolina Hinestrosa– National Breast Cancer Coalition

Written Submission:
Barbara A. Brenner, Executive Director, Breast Cancer Action

The agenda was as follows:

Call to Order and Introductions	**Maha Hussain, M.D.** Committee Chair Oncologic Drugs Advisory Committee
Conflict of Interest Statement	**Nicole Vesely, Pharm.D.** Designated Federal Official Oncologic Drugs Advisory Committee
Opening Remarks	**Richard Pazdur, M.D.** Director, Office of Oncology Drug Products FDA Center for Drug Evaluation and Research

==========

Metastatic Breast Cancer Treatments	**Patricia Cortazar, M.D.** Medical Officer, Division of Drug Oncology Products OODP,OND,CDER,FDA

Sponsor Presentation – Genentech, Inc.

Overview	**David Schenkein, M.D.** Sr. Vice Presdient Clinical Hematology&Oncology Genentech, Inc.
ECOG E2100- Study Design and Efficacy	**Kathy Miller, M.D.** Associate Professor of Medical Oncology Indiana University School of Medicine
ECOG E2100- Safety	**Barbara Klencke** Associate Group Medical Director Genentech, Inc.
Metastatic Breast Cancer and Avastin: Placing ECOG Study 2100 in Context	**Eric Winer, M.D.** Associate Professor Department of Medicine Harvard Medical School
Concluding Remarks	**Christopher Bowden, M.D.** Senior Group Medical Director Genentech, Inc.
FDA Presentation: Bevacizumab (Avastin®) plus Paclitaxel for 1st line Metastatic Breast Cancer	**sBLA 125085/91** **Lee Pai-Scherf, M.D.** Medical Officer, Division of Biologic Oncology Products, OODP, OND, CDER, FDA and **Laura Lu, Ph.D.** Statistical Reviewer- Biologic Oncology, Division of Biostatistics 5, Office of Biostatistics, CDER, FDA

Open Public Hearing

Questions from Committee

Questions to the ODAC
and ODAC Discussion

Adjourn

Questions to the committee:

1. In the E2100 study, PFS is not a surrogate endpoint for overall survival (OS) in first-line breast cancer. Please discuss whether PFS alone without a demonstrated survival advantage should be considered a measure of direct clinical benefit in the initial treatment of metastatic breast cancer. (Non-voting question)

The committee was asked to discuss the aforementioned question with no vote being required. The committee's comments are summarized as follows:

- *The committee agreed that there was concern over the toxicity profile of Avastin and if the product would do more harm than good to patients. A question was raised as to whether a distinction should be made as to the acceptability of the toxicity in 2nd or 3rd line metastatic breast cancer versus first line.*

- *One committee member mentioned that many of the women in the E2100 trial were pre-treated so very few were truly receiving 1st line therapy making it hard to reach the overall survival (OS) endpoint. This member also mentioned that it would be helpful to identify the subsets of patients who would benefit from this therapy. A few other committee members agreed with this statement.*

- *The committee expressed concerns that theE2100 study had shortcomings and inconsistencies such as data collection and imaging discordance. Also, concern was expressed that specific definition for bone progression was not used to ensure objectivity considering the percentage of patients with bone disease.*

- *Many committee membes agreed that Progression Free Survival is a clinically meaningful endpoint but had issues with how best to measure this endpoint. Although the overall survival (OS) endpoint was not met, most felt that no progression is better than progression in the minds of patients. The committee also reaffirmed that if PFS is to be used then studies must also be powered for survival to ensure that benefit out way the risks. One committee member mentioned that an overall survival requirement in 1st line breast cancer is difficult to achieve due to challenges with monitoring.*

Please see the transcript for detailed discussion.

2. Summary results:
    - Estimated 5.5 month improvement in median PFS claimed by Genentech
    - No improvement in OS
    - Increased toxicity/toxic death
    - No effect on PFS or OS in 2nd and 3rd line MBC

Are the data provided sufficient to establish a favorable risk/benefit analysis for the use of bevacizumab plus paclitaxel for first-line treatment of patients with metastatic breast cancer ? (Voting Question)

Vote : Yes=4 No = 5 Abstain = 0

Prior to the vote, the committee was asked to discuss this question. The committee's comments are summarized as follows:

- *The committee members expressed concerns over the toxicity of Avastin with one committee member mentioning that some of these toxicities are specific to Avastin and others are due to additional therapy*

- *One committee member mentioned that the data may not favor approval of the product due to missing data and that patients should not be offered false hope if the data is not complete. Other members agreed that issues with data collection were present. One member mentioned that there were deficiencies in the application and that other agents were available in this setting.*

Please see the transcript for detailed discussion.

The session adjourned @ approximately 2:45 p.m.