**Summary Minutes of the**
**Oncologic Drugs Advisory Committee**
**March 31, 2009**
**Location: Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland.**

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

**These summary minutes for the March 31, 2009 Meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on ____4/9/2009_____.**

**I certify that I attended the March 31, 2009 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/_____**
Wyndham Wilson, M.D.
Acting Committee Chair

The Oncologic Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on March 31, 2009 at the Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. 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 Wyndham Wilson, M.D. (Acting Committee Chair); the conflict of interest statement was read into the record by Nicole Vesely, Pharm.D. (Designated Federal Official). There were approximately 225 persons in attendance. There were twelve (12) speakers for the Open Public Hearing session.

**Issue:** The committee will discuss supplemental biologic license application (sBLA) 125085/169, Avastin (bevacizumab), Genentech, Incorporated, proposed indication as single agent, for the treatment of previously treated glioblastoma multiforme.

**Attendance:**

**Oncologic Drug Advisory Committee Members Present (Voting):**
Wyndham Wilson, M.D. (Acting Committee Chair), Michael Link, M.D., Virginia Mason, RN (Consumer Representative), David Harrington, Ph.D., Gary Lyman, M.D., Ronald Richardson, M.D.

**Special Government Employee Consultants (Temporary Voting Members):**
Peggy Almgren (Patient Representative), Frederick Barker, M.D., Mark Kieran, M.D., Ph.D., Jay Loeffler, M.D., F.A.C.R.

**Special Government Employee Consultant (Non-Voting):**
Erini Makariou, M.D.

**Non-voting Participants:**
Gregory Curt, M.D. (Industry Representative)
Victor Levin, M.D. (Guest Speaker)

**Oncologic Drugs Advisory Committee Members Not Present:**
S. Gail Eckhardt, M.D. (Chair)
Jean Grem, M.D., F.A.C.P.
Margaret Tempero, M.D.

**FDA Participants (Non-Voting):**
Richard Pazdur, M.D., Patricia Keegan, M.D., Lee Pai-Scherf, M.D., Sandra Casak, M.D., Yuan Li Shen, Dr. P.H.

**Designated Federal Official:**
Nicole Vesely, Pharm.D.

**Open Public Hearing Speakers:**
Max Wallace, Chief Executive Officer, Accelerate Brain Cancer Cure (ABC2)
Harriet Patterson, Director of Patient Services, National Brain Tumor Society
Thomas P. Ward, Brad Kaminsky Foundation for Brain Tumor Research
Jenny McDevitt
Richard Oropeza Jr.
BethAnn Telford, Survivor&Founder, TEAM BT-Race for Hope DC-2009
Jennifer Brusstar, CEO and President, The Tug McGraw Foundation
Gail McWilliams

Al Musella, DPM, President, Musella Foundation For Brain Tumor Research & Information, Inc.
Evonne Stevenson Schott
Lindsay Zortman, M.A.
Ann M. Levy-Oropeza

***The agenda was as follows:***

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| Call to Order<br>Introduction of Committee | **Wyndham Wilson, M.D.**<br>Acting Chair, ODAC |
| Conflict of Interest Statement | **Nicole Vesely, Pharm.D.**<br>Designated Federal Official, ODAC |
| **FDA Presentation**<br>Regulatory History and Product Approvals for GBM | **Sandra Casak, M.D.**<br>Staff Fellow, Division of Biologic Oncology Products (DBOP), OODP, OND, CDER, FDA |
| **Guest Speaker**<br>Treatment of CNS Radiation Necrosis with Bevacizumab, an Anti-VEGF Antibody | **Victor Levin, M.D.**<br>Professor and Bernard W. Biedenharn Chair for Cancer Research, Department of Neuro-Oncology, The University of Texas MD Anderson Cancer Center |
| **Sponsor Presentation**<br>Introductions | **Genentech Inc.**<br>**David Schenkein, M.D.**<br>Sr. Vice President, Clinical Hematology and Oncology<br>Genentech Inc. |
| MR Imaging in Glioblastoma | **A. Gregory Sorensen, M.D.**<br>MGH-HST Center for Biomarkers in Imaging<br>A. A. Martinos Center, Massachusetts General Hospital<br>Harvard Medical School & Massachusetts Institute of Technology<br>Division of Health Sciences and Technology |
| Study AVF3708g and NCI 06-C-0064E | **Julie Hambleton, M.D.**<br>Associate Group Medical Director<br>Genentech Inc. |
| Avastin Study in Context | **Michael Prados, M.D.**<br>Charles B. Wilson Professor of Neurosurgery,<br>Director of Division of Translational Research,<br>University of California San Francisco<br>Project Leader: North American Brain Tumor Consortium (NABTC) |
| Conclusions | **David Schenkein, M.D.**<br>Sr. Vice President, Clinical Hematology and Oncology<br>Genentech Inc. |
| **FDA Presentation**<br>Bevacizumab (Avastin) for | **sBLA 125085/169**<br>**Lee Pai-Scherf, M.D.** |

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|---|---|
| Previously Treated Glioblastoma Multiforme | Medical Officer, Division of Biologic Oncology Products, (DBOP), OODP, OND, CDER, FDA |
| | **Yuan Li Shen, Dr. P.H.**<br>Statistical Reviewer - Biologic Oncology,<br>Division of Biostatistics 5 (DB5), Office of Biostatistics (OB), Office of Translational Science (OTS), CDER, FDA |

Questions to the Presenters

Open Public Hearing

Questions to the ODAC and ODAC Discussion

Adjourn

***Questions to the committee:***

QUESTION # 1 (For discussion)

GBM are morphologically heterogeneous tumors with varying amounts of necrosis and edema. Due to the diffusely infiltrative nature of the tumor and the presence of surrounding edema, measurement of enhancing lesions on MRI is problematical. This difficulty is even greater for relapsed gliomas after prior surgery and radiation therapy, the target population for this application.

In addition, bevacizumab neutralizes VEGF-induced vascular permeability, stabilizes the blood-brain barrier, decreasing extravasation of fluid into brain parenchyma and results in reduced edema and decreased corticosteroid requirements. It is unclear whether the radiographic improvement accompanied by a decreased requirement for steroids reported in this application is the result of an anti-tumor effect of bevacizumab or represents radiographic improvement due to reduction in tumor associated edema and radiation induced necrosis, or both.

For these two reasons, the value of using objective response determined by standard MRI as surrogate endpoint for survival in GBM is unclear.

Please discuss the validity of objective response as determined by standard MRI, in the setting of VEGF inhibition to support accelerated approval of GBM.

*Discussion:*

- *The committee agreed the population in question did not have many treatment options.*
- *Overall, the committee was unsure if the changes on the radiographic images were due to changes in vascular permeability and/or reduction in tumor but felt that the changes resulted in a positive benefit in respect to symptoms based on the decreased steroid requirement and anecdotal reports.*
- *Many committee members felt that any future trials should be powered to measure quality of life.*

- *Some members questioned whether future trials will show an advantage in overall survival.*
- *It was noted that more safety data for this population needed to be provided.*

Please see the transcript for detailed discussion.

QUESTION # 2 (Voting)

Objective response has not been used as the basis for accelerated approval for GBM.

Objective response rate as determined by standard MRI, was 25.9% and 19.6% in two single arm studies. The median duration of response for responders was 4.2 months and 3.9 months, respectively. There were no complete responses.

Is the response seen in this application of sufficient magnitude (i.e., clinically meaningful) to serve as a surrogate reasonably likely to predict clinical benefit for the purpose of accelerated approval in refractory GBM?

***Vote :*** ***Yes=10*** ***No = 0*** ***Abstain = 0***

Please see the transcript for detailed discussion.

The meeting adjourned @ approximately 2:15 p.m.