



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: September 12, 2008

To: NCCTG Primary Clinical Research Associates

From: Sara Braun

Re: N0775, A Randomized Phase II Trial of Temozolomide (TMZ) and Avastin® or ABI-007/Carboplatin (CBDCA) and Avastin® in Patients with Unresectable Stage IV Malignant Melanoma

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with Bevacizumab for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

AE_265033

Please note that all risks currently cited in the NCCTG consent form cannot be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

Please submit this adverse event to your Institutional Review Board.

If you have any questions concerning this communication, please contact Sara Braun at braun.sara@mayo.edu or 507-538-8226.

SB/kjm
enclosure

Genentech

IN BUSINESS FOR LIFE

Date: 4 August 2008

Axel Grothey, MD

Mayo Clinic

200 First Street S.W.

Rochester, MN 55905

RE: IND Safety Report/Expedited Case Safety Report

Investigational Product(s): **Bevacizumab**

GNE MCN: **265033 Initial** Other Reference Number(s):

Dear Dr. Grothey,

Attached is a case summary of a serious and unexpected adverse drug reaction that occurred in a subject exposed to bevacizumab. Good Clinical Practice regulations require that you promptly submit a copy of this IND safety report/expedited case safety report to your Institutional Review Board or Independent Ethics Committee. File a copy of this IND safety report/expedited case safety report in your protocol file so that it is available for review during a Sponsor monitoring visit and/or regulatory audit.

In the European Economic Area (EEA) Genentech, Inc. or its designee will directly inform the Institutional Review Boards/Ethics Committees, as appropriate.

This IND safety report/expedited case safety report must be filed with your Investigator Brochure (IB) for information only. This IND safety report/expedited case safety report is not considered an addendum to your safety reference document.

Although this adverse event has been documented and reported to the appropriate Regulatory agencies, the report does not necessarily reflect a conclusion by Genentech or the Regulatory agencies that bevacizumab contributed to the adverse event.

If questions arise, please contact the undersigned.

Sincerely,



Eric Hedrick
Medical Monitor
AVF3918s AVF3870s

For use by user-facilities,
importers, distributors and manufacturers
for MANDATORY reporting

MEDWATCH
3500A Facsimile

Page 1 of 2

Mfr Report #	265033
UF/Importer Report #	
FDA Use Only	

A. PATIENT INFORMATION			
1. Patient Identifier	2. Age at Time of Event: 67 Years or Date of Birth:	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight ____ lbs or ____ kgs
In confidence			
B. ADVERSE EVENT OR PRODUCT PROBLEM			
1. <input checked="" type="checkbox"/> Adverse Event and/or <input type="checkbox"/> Product Problem (e.g., defects/malfunctions)			
2. Outcomes Attributed to Adverse Event (Check all that apply)			
<input checked="" type="checkbox"/> Death: 01/04/2008 (mm/dd/yyyy) <input type="checkbox"/> Disability or Permanent Damage <input type="checkbox"/> Life-threatening <input type="checkbox"/> Congenital Anomaly/Birth Defect <input checked="" type="checkbox"/> Hospitalization - initial or prolonged <input type="checkbox"/> Other Serious (Important Medical Events) <input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)			
3. Date of Event (mm/dd/yyyy) 12/26/2007		4. Date of This Report (mm/dd/yyyy) 07/31/2008	
5. Describe Event or Problem Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) suspicion of hemiparesis [HEMIPARESIS]			
Case Description: IND SAFETY REPORT			
This case, manufacturer control number 265033, is a report from GERMANY referring to a 67 Year-old Male subject (ID #). An Investigator reported this case from Genentech sponsored trial OSI3364G, A phase III, multicenter, placebo-controlled, double-blind, randomized clinical trial to evaluate the efficacy of bevacizumab in combination with tarceva compared with tarceva alone for treatment of advanced non-small cell lung cancer (NSCLC) after failure of standard first-line chemotherapy.			
continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates			
7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) Race: Caucasian			

C. SUSPECT PRODUCT(S)			
1. Name (Give labeled strength & mfr/labeler)			
#1. BEVACIZUMAB OR PLACEBO (Bevacizumab) (Continued)			
#2. Erlotinib (ERLOTINIB) Tablet, 150mg			
2. Dose, Frequency & Route Used		3. Therapy Dates (if unknown, give duration from/to (or best estimate))	
#1. 1260 mg, Q3W, Intravenous		#1. 11/08/2007 to UNK	
#2. 150 mg, qd, Oral		#2. 11/08/2007 to UNK	
4. Diagnosis for Use (Indication)		5. Event Abated After Use Stopped or Dose Reduced? (Doesn't Apply)	
#1. nsclc (NSCLC)		#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
#2. nsclc (NSCLC)		#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
6. Lot #	7. Exp. Date	8. Event Reappeared After Reintroduction? (Doesn't Apply)	
#1. 4(Continued)	#1.	#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
#2. PT9498T29	#2.	#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
9. NDC# or Unique ID			
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
G. ALL MANUFACTURERS			
1. Contact Office - Name/Address (and Manufacturing Site for Devices) Genentech, Inc. James Nickas Pharm.D. 1 DNA Way South San Francisco, CA 94080 UNITED STATES			2. Phone Number 6502255591
4. Date Received by Manufacturer (mm/dd/yyyy) 07/25/2008			3. Report Source (Check all that apply) <input checked="" type="checkbox"/> Foreign DEU <input checked="" type="checkbox"/> Study <input type="checkbox"/> Literature <input type="checkbox"/> Consumer <input checked="" type="checkbox"/> Health Professional <input type="checkbox"/> User Facility <input checked="" type="checkbox"/> Company Representative <input type="checkbox"/> Distributor <input type="checkbox"/> Other:
6. If IND, Give Protocol # OSI3364G		5. (A)NDA # IND # BB 7023 STN # PMA/510(k) #	
7. Type of Report (Check all that apply) <input type="checkbox"/> 5-day <input type="checkbox"/> 30-day <input type="checkbox"/> 7-day <input type="checkbox"/> Periodic <input type="checkbox"/> 10-day <input checked="" type="checkbox"/> Initial <input checked="" type="checkbox"/> 15-day <input type="checkbox"/> Follow-up #		Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
9. Manufacturer Report Number 265033		8. Adverse Event Term(s) HEMIPARESIS	
E. INITIAL REPORTER			
1. Name and Address			Phone #
2. Health Professional?	3. Occupation	4. Initial Reporter Also Sent Report to FDA	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Unk	

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

MEDWATCH

3500A Facsimile (Back) (Continued)

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Mfr Report #	265033
UF/Importer Report #	
	FDA Use Only

ADDITIONAL INFORMATION**B5. EVENT DESCRIPTION (Continued)**

On 08-NOV-2007, the subject began treatment with BEVACIZUMAB OR PLACEBO (1260 mg, Q3W, Intravenous) and ERLOTINIB (150 mg, qd, Oral). The lot numbers for BEVACIZUMAB OR PLACEBO was reported as 41559, 41565, and 41555. The lot number for Erlotinib was reported as PT9498T29. The last dose of BEVACIZUMAB OR PLACEBO prior to the onset of the event was administered on 09-NOV-2007. The last dose of Erlotinib prior to the onset of the event was administered on 29-NOV-2007.

On 26-DEC-2007, the subject was hospitalized with suspicion of hemiparesis (HEMIPARESIS). No relevant laboratory or diagnostic tests were reported. Treatment for the event was reported as unknown.

On 04-JAN-2008, the subject expired due to hemiparesis. It was unknown if an autopsy was performed. The action taken with Bevacizumab or placebo and Erlotinib was not applicable.

The Investigator assessed the event hemiparesis as related to Bevacizumab or Placebo and not related to Erlotinib. In the reporter's opinion, other possible etiological factors included the subject's disease under study.

On 29-JUL-2008, the subject was unblinded to Bevacizumab.

This report contains case details known at the time of the submission.

Additional follow up is being requested. If received, the case will be updated accordingly.

PREVIOUSLY FILED IND SAFETY REPORTS OF SIMILAR EVENTS:

Genentech has not filed previous IND safety reports of hemiparesis for subjects receiving Bevacizumab.

SPONSOR ASSESSMENT

Based on review of available data, no compelling evidence of a cause-and effect-relationship between administration of Bevacizumab and the occurrence of hemiparesis can be identified.

At this time, the Sponsor does not believe changes to the conduct of this clinical trial are warranted.

C1. NAME (Continued)

Suspect Medication #1: BEVACIZUMAB OR PLACEBO(Bevacizumab) Powder and solvent for solution for infusion, 100mg

C6. LOT# (Continued)

Suspect Medication #1: 41559, 41565, 41555

ADDITIONAL INFORMATION**7+13. DESCRIBE REACTION(S) continued**

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14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) BEVACIZUMAB OR PLACEBO (Bevacizumab) Powder and solvent for solution for infusion, 100 mg (Lot # 41559, 41565, 41555); Regimen #1	1260 mg, Q3W; Intravenous	nsclc (NSCLC)	08-NOV-2007 / Unknown; Unknown

25b. Name And Address of Reporters continued

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)

15. DAILY DOSE(S)
16. ROUTE(S) OF ADMIN

17. INDICATION(S) FOR USE

18. THERAPY DATES (from/to);
19. THERAPY DURATION
