



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** October 19, 2007  
**To:** NCCTG Primary Clinical Research Associates  
**From:** Lori Bratvold  
Protocol Development Coordinator  
**Re:** N0177, A Phase I/II Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with OSI-774 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\_248756**

Please note that all risks currently cited in the NCCTG consent form can not 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 Janis Wobschall at [wobschall.janis@mayo.edu](mailto:wobschall.janis@mayo.edu) or 507-284-4852.

JW/df  
enclosure

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

**MEDWATCH**  
3500A Facsimile

Mfr Report #	248756
UF/Importer Report #	
FDA Use Only	

A. PATIENT INFORMATION			
1. Patient Identifier	2. Age at Time of Event: 57 Years or Date of Birth:	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight 167.0 lbs or 75.7 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 10/01/2007 (mm/dd/yyyy)		<input type="checkbox"/> Disability or Permanent Damage	
<input type="checkbox"/> Life-threatening		<input type="checkbox"/> Congenital Anomaly/Birth Defect	
<input 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) 10/01/2007		4. Date of This Report (mm/dd/yyyy) 10/10/2007	
5. Describe Event or Problem Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) death[DEATH]			
Case Description: IND SAFETY REPORT			
This case, manufacturer control number 248756, is a report from the UNITED STATES referring to a 57 Year-old Male subject (id # ). An investigator reported this case from study AVF3671g-B, a randomized, double blind, placebo controlled, phase IIIb trial comparing bevacizumab therapy with or without erlotinib after completion of chemotherapy with bevacizumab for the first line treatment of locally advanced, recurrent, or metastatic non-small cell lung.			
The subject is enrolled in the post-chemotherapy phase of trial AVF3671g and began treatment with bevacizumab (1200 mg, Q3W, Intravenous) on 08-NOV-2006. The lot number was N38279. continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates NI			
7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) NI			

C. SUSPECT PRODUCT(S)	
1. Name (Give labeled strength & mfr/labeler)	
#1. ERLOTINIB OR PLACEBO(Erlotinib) Tablet	
#2. Bevacizumab(BEVACIZUMAB) Powder and solvent for (continued)	
2. Dose, Frequency & Route Used	3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. 150 mg, qd, Oral	#1. 02/01/2007, duration UNK
#2. 1200 mg, Q3W, Intravenous	#2. 11/08/2006, duration UNK
4. Diagnosis for Use (Indication)	5. Event Abated After Use Stopped or Dose Reduced?
#1. non-small cell lung (continued)	#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply
#2. non small cell lung (continued)	#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply
6. Lot #	7. Exp. Date
#1. 2004739	#1. UNK
#2. N38279	#2. UNK
9. NDC # or Unique ID	
8. Event Reappeared After Reintroduction?	
#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event) NI	

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) 10/02/2007	3. Report Source (Check all that apply) <input type="checkbox"/> Foreign <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 type="checkbox"/> Company Representative <input type="checkbox"/> Distributor <input type="checkbox"/> Other:
5. (A)NDA # IND # US BB 7023 STN # PMA/ 510(k) # Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
6. If IND, Give Protocol # AVF3671G-B	
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 #	
9. Manufacturer Report Number 248756	8. Adverse Event Term(s) DEATH

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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Mir Report #	248756
UF/Importer Report #	
	FDA Use Only

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

On 01-FEB-2007, the subject began treatment with erlotinib or placebo (150 mg, qd, Oral). The lot number was 2004739. The last dose of bevacizumab prior to the event was administered on 19-SEP-2007. The last dose of erlotinib or placebo prior to the event was unknown.

On 01-OCT-2007, the subject was found dead (DEATH) at home. No relevant laboratory data was reported, it was unknown if an autopsy was preformed. There was no treatment for the event. The action taken with bevacizumab and erlotinib or placebo was not applicable.

On 4-OCT-2007, the subject was unblinded to erlotinib.

The Investigator assessed the event death as related to erlotinib and bevacizumab. There were no other suspected causes of the event.

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

Additional information has been requested.

**Pharmacovigilance:**

DEATH is unlabeled in the USPI and unexpected in the IB for BEVACIZUMAB, and unexpected in the IB for ERLOTINIB. A report of death occurring after initiating bevacizumab therapy with unblinded erlotinib administered for non-small cell lung cancer in a 57 Year-old Male subject from the UNITED STATES participating in a study. The event is assessed as related to both drugs. Confounding factors include the possibility of progression of underlying condition.

**C1. Name (Continued)**

Suspect Medication #2: Bevacizumab(BEVACIZUMAB) Powder and solvent for solution for infusion, 100mg

**C4. Diagnosis for use (Continued.)**

#1:non-small cell lung cancer(NON-SMALL CELL LUNG CANCER)

#2:non small cell lung cancer(NON SMALL CELL LUNG CANCER)



**ADDITIONAL INFORMATION**

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

The subject is enrolled in the post-chemotherapy phase of trial AVF3671g and began treatment with bevacizumab (1200 mg, Q3W, Intravenous) on 08-NOV-2006. The lot number was N38279. On 01-FEB-2007, the subject began treatment with erlotinib or placebo (150 mg, qd, Oral). The lot number was 2004739. The last dose of bevacizumab prior to the event was administered on 19-SEP-2007. The last dose of erlotinib or placebo prior to the event was unknown.

On 01-OCT-2007, the subject was found dead (DEATH) at home. No relevant laboratory data was reported, it was unknown if an autopsy was performed. There was no treatment for the event. The action taken with bevacizumab and erlotinib or placebo was not applicable.

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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 ERLOTINIB OR PLACEBO (Erlotinib) Tablet {Lot # 2004739}; Regimen #1	150 mg, qd; Oral	non-small cell lung cancer(NON-SMALL CELL LUNG CANCER)	01-FEB-2007 00:00 / Unknown; Unknown
#2 Bevacizumab (BEVACIZUMAB) Powder and solvent for solution for infusion, 100 mg {Lot # N38279}; Regimen #1	1200 mg, Q3W; Intravenous	non small cell lung cancer(NON SMALL CELL LUNG CANCER)	08-NOV-2006 00:00 / Unknown; Unknown