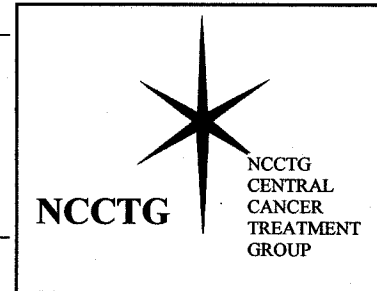

Operations Office

Telephone (507) 266-3549



Date: July 8, 2005

To: NCCTG Primary Clinical Research Associates

From: Lori K. Kelly
Protocol Development Coordinator

Re: N0272, Phase II Trial of STI-571 in Treatment of Recurrent Oligodendroglioma and Mixed Oligoastrocytoma

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with STI-571 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_PHHO2005BE09601

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 Lori K. Kelly at 507/266-3549.

lkk
enclosure

To: All Investigators in Imatinib (STI571) Studies*

DATE: June 28th, 2005

Re: Investigator Notification for Imatinib (STI571)

Manufacturer Case ID PPHO2005BE09601

Muscle Rent, Pain in Extremity, Edema

Study CSTI571ADE22

Dear Doctor,

In accordance with the Good Clinical Practice and specific national regulatory requirements, we wish to inform you of a serious, unexpected, possibly related adverse event of Muscle Rent that occurred in a 54-year-old male treated with Imatinib (STI571) in study protocol CSTI571 ABE01.

For the current case details are provided in the attached CIOMS I form, which contains the initially available information reported to Novartis.

To summarize,

This patient was enrolled in study protocol CSTI571ABE01, a phase II, open label, non-randomized, multicenter study to determine the safety and efficacy of imatinib mesylate in patients with idiopathic hypereosinophilic syndrome. He received his first dose of study medication on 26 Apr 2003. Medical history: Hypertension, anxiety, depression and Parkinson's disease. On 07 Apr 2005 the patient experienced muscular rent (right leg) with right leg pain and edema and was hospitalised. On 20 May 2005 the patient experienced muscular rent (left leg) with left leg pain and edema and was again hospitalised. At the time of this report (17 Jun 2005) the patient's condition was unchanged. Initially the investigator did not suspect a relationship between the muscular rent (right leg) and the study medication, but having regard for the recurrence contra laterally he re-assessed the causality as "suspected".

A search of the manufacturer's safety database did not show any previous reports of muscular injury with Imatinib. The sponsor believes that the present report is possibly confounded by the indication "hypereosinophilic syndrome", which might cause muscular involvement in some cases. Muscle injury has not become apparent as a side effect of Gleevec during the use for CML or GIST.

We will keep you informed if further medically significant information becomes available that is relevant to this event or if any additional action is necessary. We ask that you please inform your Institutional Review Board or Ethics Review Board of this event, if you have such an obligation.

Yours sincerely,

Richard Pilot, MD, MSc (Epid.), MPH
Senior Director, Clinical Safety and Epidemiology
Novartis Pharmaceutical Corporation
One Health Plaza
East Hanover, NJ, 07936
United States of America

Attachment: CIOMS case report

* Novartis Investigator Notification: International Guidelines for Good Clinical Practice as well as specific health authority regulations require that clinical investigators be informed of any adverse drug reaction which is serious (according to specific regulatory criteria), unexpected (i.e. not specifically mentioned in the Investigator's Brochure) and which has a 'reasonable possibility' (in the opinion of the reporter and/or the Company) of being related to the study medication. While Novartis tries to obtain all meaningful information as soon as possible, we are required to communicate all available information within a specified time of its receipt. Since initial data is frequently incomplete, further information must be sent in the form of follow-up reports. Where they have such an obligation, investigators are expected to inform institutional review boards/ethics committees, of each investigator notification. Should Novartis believe that a change in protocol or other action needs to be taken on the basis of clinical reports or other available data, the company will communicate such changes to involved investigators.

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year	54 Years	Male	104.00 kg	Day	Month	Year	
		25	AUG	1950				07	APR	2005	<input type="checkbox"/> PATIENT DIED <input checked="" type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION <input type="checkbox"/> INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY <input type="checkbox"/> LIFE THREATENING
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) Musculary rent [Muscle injury] ([Pain in extremity], [Oedema]) Case Description: Initial report received 17 Jun 2005: This patient (centre number xx, patient number xx) was enrolled in study protocol CSTI571 ABE01, a phase II, open label, non-randomized, multicenter study to determine the safety and efficacy of imatinib mesylate (STI571 - Glivec®) in patients with idiopathic hypereosinophilic syndrome. He received his first dose of the study medication on 26 Apr 2003. Medical history: Hypertension, anxiety, depression and Parkinson's disease. On 07 Apr 2005 the patient experienced musculary rent (right leg) with right leg pain and edema and was hospitalised. (continue)											

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name) #1 CGP 57148B(STI571/CGP57148B T35717+CAPS)Capsule		20. DID REACTION ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA
15. DAILY DOSE(S) #1 100mg every two days	16. ROUTE(S) OF ADMINISTRATION #1 Oral	
17. INDICATION(S) FOR USE #1 Hypereosinophilic syndrome		21. DID REACTION REAPPEAR AFTER REINTRODUCTION? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA
18. THERAPY DATES(from/to) #1 26-APR-2003 00:00 / Ongoing	19. THERAPY DURATION #1 Unknown	

III. CONCOMITANT DRUG(S) AND HISTORY (Continued on Additional Information Page)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)		
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)		
From/To Dates	Type of History / Notes	Description
Unknown		Hypertension
Unknown		Anxiety

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER Novartis Pharma Headquarter		26. REMARKS
24b. MFR CONTROL NO. PHHO2005BE09601		
24c. DATE RECEIVED BY MANUFACTURER 17-JUN-2005	24d. REPORT SOURCE <input checked="" type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input checked="" type="checkbox"/> HEALTH PROFESSIONAL <input type="checkbox"/> OTHER:	25b. NAME AND ADDRESS OF REPORTER
DATE OF THIS REPORT 28-JUN-2005	25a. REPORT TYPE <input checked="" type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP	

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

On 20 May 2005 the patient experienced musculary rent (left leg) with left leg pain and edema and was again hospitalised. At the time of this report (17 Jun 2005) the patient's condition was still present and unchanged. Initially the investigator did not suspect a relationship between the musculary rent (right leg) and the study medication, but having regard for the interval between the events in the right and left leg, the investigator re-assessed the causality as "suspected".

Novartis Comment: Serious adverse event report, (involving significant disability or incapacity), assessed as unexpected according to the Investigator's Brochure.

The information provided in this individual case does not warrant a change to the Investigator's Brochure text. The topic will be monitored closely. Investigator causality is suspected.

13. Relevant Tests

(Date unknown) Echography: Musculary rent

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		Depression
Unknown		Parkinson's disease