



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** April 28, 2006

**To:** NCCTG Primary Clinical Research Associates

**From:** Lori K. Bratvold  
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\_PHHO2006IT03299

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. Bratvold at 507/266-3549.

lkb  
enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health  
National Cancer Institute  
Bethesda, Maryland 20892

**DATE:** April 17, 2006

**FROM:** A. Dimitrios Colevas, M.D., Investigational Drug Branch, CTEP, DCTD, NCI

**SUBJECT:** STI571 (Imatinib) Investigator Notification: **Vasculitis**  
Novartis Report #PHHO2006IT03299

**TO:** Investigators of CTEP-sponsored Trials Using STI571 (NSC 716051)

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. An investigator notification, which describes vasculitis in a patient participating in a Novartis-sponsored clinical study utilizing the investigational agent STI571 (NSC 716051), was recently distributed to investigators.

The following must be completed by all investigators using STI571 under NCI IND 61135:

- Send a copy of this letter to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of this letter in your protocol file.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

CTEP's evaluation of this IND Safety Report in light of previous experience with STI571 does not require a change in the clinical protocols for this agent at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The Dear Doctor Letter and Suspect Adverse Reaction Report that describe the following adverse event are attached:

A 64-year-old female with acute lymphoblastic leukemia developed vasculitis while participating in a compassionate use study utilizing the investigational agent STI571.

There have been no incidences of vasculitis reported to the NCI as serious adverse events under the STI571 NSC 716051.

A total of 2971 patients have been enrolled in NCI-sponsored trials under the STI571 NSC 716051.

CONFIDENTIAL

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To: All Investigators in Imatinib (STI571) Studies\*

DATE: 30 March 2006  
Re: Investigator Notification for Imatinib (STI571)  
Manufacturer Case ID PHHO2006IT03299  
Vasculitis  
Study CSTI571B C/USE

Dear Doctor,

In accordance with the Good Clinical Practice and specific national regulatory requirements we wish to inform you of a serious unexpected and possibly related adverse event which occurred during the use of STI571 in compassionate use.

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

To summarize,

A 64-year-old female patient entered the study with a diagnosis of BCR/ABL positive acute lymphoblastic leukaemia. She received the first dose of study medication on 09 Jan 2006. On 15 Feb 2006 she experienced diffuse skin erythema and fever (max 38.5 degrees Celsius). Study medication was temporarily interrupted on 17 Feb 2006. A diagnosis of suspected vasculitis was made on clinical grounds; however a final diagnosis or a skin biopsy was not available. Treatment for the event included prednisone. At the time of this report (17 Mar 2006) the patient's condition was improving. The event was suspected to be related to the study medication.

A review of the Novartis safety database revealed one additional clinical trial SAE of cutaneous vasculitis in a CML patient in the accelerated phase that was suspected to be related to imatinib.

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.

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Sincerely,

Richard Pilot, MD, MPH  
GMSE, 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.



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**ADDITIONAL INFORMATION**

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

The investigator did suspect a relationship between this event and the study medication.

Follow-up received on 20 Mar 2006: The patient entered the study with a diagnosis of BCR/ABL positive acute lymphoblastic leukaemia. A diagnosis of suspected vasculitis was made, however the final diagnosis was not available. Treatment for this event included prednisone. At the time of this report (17 Mar 2006) the patient's condition was improving. This event was considered to have involved persistence of significant disability or incapacity and was suspected to be related to the study medication.

Novartis Comment: Serious adverse event report, (Disability), 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. The topic will be monitored closely.

Investigator causality is suspected.