

# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** March 9, 2007  
**To:** NCCTG Primary Clinical Research Associates  
**From:** Janis Wobschall  
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\_1458018\_F1**

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/dkf  
enclosure



DATE: March 5, 2007

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

SUBJECT: STI571 (Imatinib Mesylate, Gleevec<sup>®</sup>) NCI IND Safety Report, AE# 1458018,  
*Follow-up #1*

TO: Investigators Using CTEP-supplied Investigational STI571, IND 61135

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. Please find attached a copy of an IND Safety Report recently submitted to the FDA for the CTEP-sponsored investigational agent STI571.

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

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

If your study is not covered under IND 61135, it is strongly recommended that you follow the instructions above.

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 Adverse Events Assessment that describes the following adverse event, previous experience under this IND and/or NSC, and the total number of patients enrolled in trials under this IND and/or NSC is attached:

A 16-year-old male with chronic myelogenous leukemia experienced grade 3 bone pain while on a phase 2 trial utilizing the investigational agent STI571.

*The attached Adverse Events Assessment has been amended to correct information. Changes are indicated by bold and italics for additions and strikethrough for deletions. If this report or the Adverse Events Assessment is changed further, we will notify your office.*

**ADVERSE EVENTS ASSESSMENT**

IND 61135 NSC 716051 STI571 (imatinib mesylate, Gleevec™)	ADVERSE EXPERIENCE REPORT NO. 40 IND Safety Report: <i>Follow-up #1</i> Event: Gr. 3: Bone pain
AE: 1458018	Protocol: AAML0123

*This report has been amended to correct information. Changes to the original summary are indicated by bold and italics (new information) and/or strikethrough (deleted information). If this assessment is changed further, we will notify your office. Please note that this modified report will be distributed to investigators.*

The patient is a 16-year-old male with chronic myelogenous leukemia (CML) who experienced bone pain while on a phase 2 trial utilizing the investigational agent STI571. He began his first course of treatment on June 12, 2006, receiving STI571 570 mg/m<sup>2</sup>/day PO divided into a morning and evening dose, on Days 1-28, every 28 days. Prior to the event, he received the last dose of STI571 on December 5, 2006 (Cycle 7, Day 9).

The patient was initially diagnosed with Philadelphia chromosome positive CML in May 2006 and is status post hydroxyurea therapy. He began the investigational therapy on June 12, 2006 and completed six cycles. He began Cycle 7 on November 27, 2006. On December 5, 2006 (Cycle 7, Day 9), the patient presented to the clinic with severe right lower leg and heel pain. He was initially treated with Vicodin®; however, the pain worsened, and he was admitted to the hospital later that day where morphine and ibuprofen were added to his pain control regimen. His WBC count at admission was 12.7×10<sup>3</sup>/mm<sup>3</sup> (reference range: 4.5-11.0×10<sup>3</sup>/mm<sup>3</sup>), which was increased from a baseline count of 11.5×10<sup>3</sup>/mm<sup>3</sup>. STI571 was withheld, and his morphine dose was increased. An MRI of the right tibia and fibula on December 6, 2006 showed a possible acute bone infarction or infection. An MRI of the right ankle also performed that day was suggestive of bone marrow edema with enhancement within the calcaneus, as well as mild periosteal involvement. Morphine was discontinued and Dilaudid® initiated later that day. Over the next 48 hours, his condition improved; his WBC count on December 8, 2006 was 6.6×10<sup>3</sup>/mm<sup>3</sup>. On December 9, 2006, he was discharged to home, continuing on oral analgesics as needed. STI571 treatment was resumed at a reduced dose of 200 mg PO twice daily.

The patient's past medical history is significant for his disease only. ~~Medications taken at the time of the event included 6-mercaptopurine, methotrexate, prednisone/dexamethasone, 6-thioguanine, nystatin, and Sulfatrim®.~~ *The patient was not taking any other medications at the time of the event.*

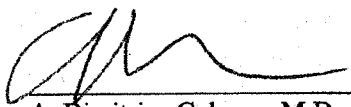
*This is the second report of grade 3 bone pain in this patient; the first report occurred during Cycle 2. However, There have been no other cases of bone pain in other patients have been reported to the NCI as serious adverse events through AdEERS under the STI571 IND.*

A total of 2861 patients have been enrolled in NCI-sponsored clinical trials under IND 61135.

In this case, it is felt that a probable relationship exists between the event and STI571 therapy.

	<b>Bone Pain</b>
STI571	Probable
Chronic myelogenous leukemia	Unlikely

Date: 3/6/07

Signature:   
A. Dimitrios Colevas, M.D.  
(IDB Monitor for STI571)

If this assessment is changed, we will notify your office.

cc: Clinical Safety & Epidemiology  
Faith Williams  
Novartis Pharmaceuticals Corporation