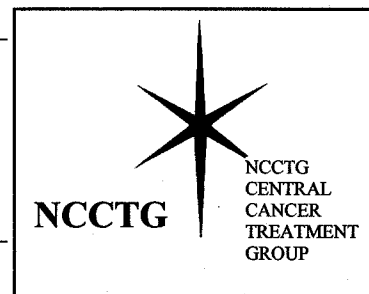


---

**Operations Office**

Telephone (507) 266-3549

---



**Date:** July 22, 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\_1365044

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.

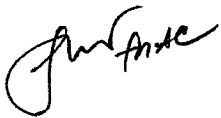
**Please submit this adverse event to your Institutional Review Board.**

If you have any questions concerning this communication, please contact Lori K. Kelly at 507/266-3549.

lkk  
enclosure



**DATE:** June 20, 2005

**FROM:** Alice Chen, M.D., Investigational Drug Branch, CTEP, DCTD, NCI 

**SUBJECT:** STI-571 (imatinib mesylate, Gleevec®) IND Safety Report, AE# 1365044

**TO:** Investigators Using 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 (IND 61135).

Please complete the following:

- 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.

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 the total number of patients enrolled in trials under this IND is attached:

The patient is a 9-year-old male with acute lymphoblastic leukemia who experienced grade 4 muscle weakness (not due to neuropathy), while on a Children's Oncology Group Pilot Study using the investigational agent STI571 (Gleevec®).

**CONFIDENTIAL**

1 of 1

\* 00003

**ADVERSE EVENTS ASSESSMENT**

IND 61135	ADVERSE EXPERIENCE REPORT NO. 29
NSC 716051	IND Safety Report:
STI571 (imatinib, Gleevec®)	Event: Gr 4: Muscle weakness (not due to neuropathy)
AE: 1365044	Protocol: AALL0031

The patient is a 9-year-old male with acute lymphoblastic leukemia who developed muscle weakness while on A Children's Oncology Group Pilot Study using the investigational agent STI571 (Gleevec®). He began his first course of STI571 treatment (consolidation block 1) on March 1, 2005. He began his cycle 4 therapy (intensification block 1) on May 3, 2005, receiving 340 mg/m<sup>2</sup> STI571 orally daily on days 1-21. He received his last dose of STI571 on May 5, 2005.

The patient was diagnosed with acute lymphoblastic leukemia in January 2005, and received multiple agent chemotherapy regimens. The patient started on the STI571 trial on March 1, 2005. On May 5, 2005, he experienced lower extremity edema, with severe muscle weakness. He was not able to walk, and he had to use a wheelchair. Three weeks prior to his muscle weakness, the patient complained of total body pain. He also experienced an episode of flat affect and a blank stare for approximately two hours. This event was thought to be related to the STI571 therapy. On May 6, 2005, he was found to be anemic. His hemoglobin was 8.7 gm/dL (reference range: 11.5-13.5 gm/dL), hematocrit 25.5% (reference range: 34-40%), and platelet count 18 K/mm<sup>3</sup> (reference range: 130-400 K/mm<sup>3</sup>). He was transfused with packed red blood cells and platelets, and his STI571 therapy was withheld. His muscle weakness was completely recovered by May 9, 2005. A bone-marrow biopsy was obtained on May 17, 2005, which showed that the patient did not relapse. As per email conversation with the site, the STI571 therapy was withheld from May 6 to May 24 and it was resumed from May 25, with a 30% dose reduction.

This patient was healthy prior to the diagnosis of acute lymphoblastic leukemia. Medications at the time of the event included dexamethasone, methotrexate, ondansetron, PEG-asparaginase, sulfamethoxazole, vincristine, cyclophosphamide, daunorubicin, G-CSF, and hydroxyzine.

There have been nine other incidences of muscle weakness (not due to neuropathy) reported to the NCI as serious adverse events under this IND. Three were assessed as unrelated, five were assessed as unlikely related, and one was assessed as possibly related to the study drug.

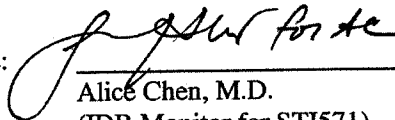
In this case, the study drug was considered possibly related to the muscle weakness (not due to neuropathy). There have been 2,234 patients enrolled in NCI-sponsored clinical trials under this IND.

	<b>Muscle weakness (not due to neuropathy)</b>
<b>STI571</b>	Possible
<b>Lymphoblastic leukemia</b>	Unlikely
<b>Dexamethasone</b>	Possible
<b>Methotrexate</b>	Unlikely
<b>Ondansetron</b>	Unlikely
<b>PEG-asparaginase</b>	Unlikely
<b>Sulfamethoxazole</b>	Unlikely
<b>Vincristine</b>	Unlikely
<b>Cyclophosphamide</b>	Unlikely
<b>Daunorubicin</b>	Unlikely
<b>G-CSF</b>	Unlikely
<b>Anemia</b>	Probable

Date:

6/20/05

Signature:



Alice Chen, M.D.  
(IDB Monitor for STI571)

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

cc: Faith Williams  
Clinical Safety and Epidemiology Department

Novartis Pharmaceuticals Corporation