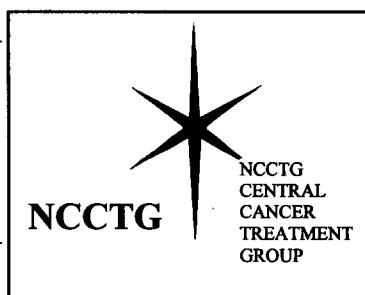

Operations Office

Telephone (507) 266-3549



Date: May 13, 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_1227958

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: April 14, 2005
FROM: Alice Chen, M.D., Investigational Drug Branch, CTEP, DCTD, NCI
SUBJECT: STI-571 IND Safety Report, AE# 1227958
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 is attached:

A 71-year-old male with gastrointestinal stromal tumor (GIST) metastatic to the liver died from infection while on a phase 2 study using the investigational agent STI571.

Infection is a known toxicity of STI571. There have been 2,144 patients enrolled in NCI-sponsored clinical trials under this IND.

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ADVERSE EVENTS ASSESSMENT

IND 61135 NSC 716051 STI571 (imatinib, Gleevec®)	ADVERSE EXPERIENCE REPORT NO. 28 IND Safety Report: Event: Gr. 5: Infection with unknown ANC
AE: 1227958	Protocol: RTOG S-0132

The patient was a 71-year-old male with gastrointestinal stromal tumor (GIST) metastatic to the liver who died from infection while on a phase 2 study using the investigational agent STI571. He began his first course of treatment on December 10, 2004 receiving STI571 600 mg orally daily. His last dose was administered on March 18, 2005 (cycle 4).

The patient was diagnosed with GIST in January 2004 and he had a complete resection of the GIST at that time. The patient was diagnosed with Parkinson's disease approximately 5 years previously, for which a cervical spine surgery was conducted without benefit. He was later found to have liver metastases from the GIST tumor. On December 10, 2004 he started treatment with STI571. He was seen by a neurologist on March 10, 2005, and it was noted that the patient had overall moderately severe bradykinesia. The patient had also experienced severe progressive dysarthria, sialorrhea, and freezing of gait associated with falls. Also of note, while eating, food had gotten stuck in the patient's throat when he attempted to swallow, but there was no apparent aspiration. He also had a 2-3 month history of hallucinations, and he requires assistance with all of his activities of daily living. On March 30, 2005 during a routine follow-up phone call, the patient's daughter-in-law reported that the patient had died on March 28, 2005. A local physician in Mexico City confirmed that the patient died of probable aspiration pneumonia. Additional medical records have been requested.

The patient's past medical history is significant for Parkinson's disease. Medications at the time of the event included Botox®, Sinemet®, Tafil®, Zofran®, Pantozol®, Rohypnol®, Akineton®, Largactil®, and Megace®.

Infection is a known toxicity of STI571. In this case, it is felt that the pneumonia definitely contributed to the infection; however a possible relationship to study drug, Botox®, Sinemet®, and Parkinson's disease cannot be excluded. The patient's GIST is considered unlikely related to the

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infection. There have been 2,144 patients enrolled in NCI-sponsored clinical trials under this IND.

	Infection with unknown ANC
STI571	Possible
GIST	Unlikely
Botox[®] injection	Possible
Sinemet[®]	Possible
Parkinson's disease	Possible
Pneumonia	Definite

Date: 4/15/05

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

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

cc: Faith Williams
Novartis Pharmaceuticals Corporation