

NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: June 22, 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_1766496


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 or 507/284-4852

JW/dkf
enclosure



DATE: June 18, 2007
FROM: Anthony J. Murgo, M.D., , Investigational Drug Branch, CTEP, DCTD, NCI
SUBJECT: STI571 (Imatinib Mesylate, Gleevec[®]) NCI IND Safety Report, AE# 1766496
TO: Investigators Using CTEP-supplied Investigational 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. 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.

Based on CTEP's assessment of the current information in light of previous experience with STI571, there does not appear to be a change in the risk-benefit ratio for STI571 studies; therefore, CTEP is not requiring a protocol amendment at this time.

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

The attached Adverse Events Assessment describes the adverse event(s) (synopsis provided below), relevant previous experience under this IND and/or NSC, and the total number of patients enrolled in trials under this IND and/or NSC.

A 50-year-old female with gastrointestinal stromal tumor experienced a bowel perforation while on a phase 2 trial utilizing the investigational agent STI571.

ADVERSE EVENTS ASSESSMENT

IND 61135 NSC 716051 STI571 (imatinib mesylate, Gleevec®)	ADVERSE EXPERIENCE REPORT NO. 45 IND Safety Report: Initial Event: Gr. 4: Bowel perforation
AE: 1766496	Protocol: RTOG S-0132

The patient is a 50-year-old female with gastrointestinal stromal tumor (GIST) who experienced a bowel perforation while on a phase 2 trial utilizing the investigational agent STI571. She began her first course of treatment on May 25, 2005 receiving STI571 600 mg PO daily for 8 weeks pre-operatively, followed by Whipple procedure, right colectomy, and extended bowel resection on October 24, 2005. She resumed therapy with STI571 within 2-4 weeks post-operatively for up to 24 months. She received her last dose of STI571 on May 10, 2007 (Cycle 8, Day 29, with a 17-day delay from April 12 through May 1, 2007).

The patient was initially diagnosed with GIST in May 2005 and began STI571 treatment on May 25, 2005. She was to begin Cycle 8 on April 12, 2007; however, STI571 therapy was delayed for 17 days secondary to an elevated glucose level (grade 2). She was cleared to continue STI571 on May 1, 2007. On May 11, 2007, the patient was hospitalized for acute onset of sharp, constant abdominal pain associated with nausea. An abdominal obstruction series was suggestive of probable pneumoperitoneum with perforation of a hollow viscus. A CT scan of the abdomen demonstrated pneumoperitoneum with mild inflammatory changes surrounding the region of anastomosis of the small bowel to the proximal end of the resected midtransverse colon and just distal to the region of anastomosis suspected to be the etiology of pneumoperitoneum. These findings were suspicious for anastomotic breakdown. The patient underwent an emergent exploratory laparotomy on the same day. A closure of the perforated bowel at the previous ileo-transverse colon anastomosis was performed, as well as lysis of multiple intestinal adhesions. Multiple nodules throughout the mesentery were concerning for possible recurrence. However, further pathologic evaluation of the biopsied ileocolic anastomosis and mesenteric mass revealed inflammation and no evidence of tumor. Post-operatively, the patient required a NG tube placement for significant nausea and abdominal pain. Her condition gradually improved, and she was able to tolerate a full diet by discharge on May 18, 2007. A decision regarding the patient's continued participation in the study is pending.

The patient's past medical history is significant for hypertension, anxiety, and recently elevated glucose levels. Medications taken at the time of the event included temazepam, aspirin, Percocet®, diazepam, Effexor®, lisinopril/hydrochlorothiazide, Prilosec®, Lipram®, Celebrex®, prochlorperazine, and multivitamin supplements.

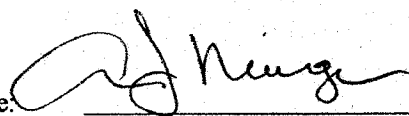
There have been no other cases of bowel perforation reported to the NCI as serious adverse events through ADEERS under the STI571 IND and NSC.

A total of 3,563 patients have been enrolled in NCI-sponsored clinical trials under the STI571 NSC.

In this case, it is felt that a possible relationship between the event and STI571 therapy cannot be excluded.

	Bowel Perforation
STI571	Possible
Surgery	Possible
GIST	Unlikely

Date: 6-19-07

Signature: 
Anthony J. Murgu, 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