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**Operations Office**

Telephone (507) 266-3549

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**Date:** August 26, 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\_1229955

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:** July 25, 2005  
**FROM:** Alice Chen, M.D., Investigational Drug Branch, CTEP, DCTD, NCI  
**SUBJECT:** STI571 (imatinib mesylate, Gleevec®) IND Safety Report, AE# 1229955  
**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 events, previous experience under this IND, and the total number of patients enrolled in trials under this IND is attached:

A 72-year-old male with metastatic Merkel cell tumor experienced grade 4 hyperglycemia and grade 3 psychosis while on a phase 2 trial using the investigational agent STI571.

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**ADVERSE EVENTS ASSESSMENT**

IND 61135 NSC 716051 STI571 (Imatinib mesylate, Gleevec®)	ADVERSE EXPERIENCE REPORT NO. # 31 IND Safety Report: Event: Gr: 4 Glucose, serum-high Gr: 3 Psychosis (hallucinations/delusions)  Protocol: S0331
AE: 1229955	

The patient is a 72-year-old male with metastatic Merkel cell tumor who experienced hyperglycemia and psychosis while on a phase 2 trial using the investigational agent STI571. He began his first course of treatment on July 7, 2005 receiving STI571 400 mg PO daily, every 28 days. He received the last dose of STI571 on July 13, 2005 (Cycle 1, Day 7).

The patient was initially diagnosed with Merkel cell carcinoma in April 2005 and had not received prior chemotherapy for his disease. He began STI571 therapy on July 7, 2005. Patient is a diabetic on insulin. His blood glucose level usually is between 100-300 md/dl. On July 14, 2005, the patient presented to the Emergency Room with hematuria, confusion, hallucinations, increasing weakness, dehydration, and decreased oral intake. Laboratory values revealed a blood glucose level of 988 mg/dL (reference range: 55-160 mg/dL), which had increased from his baseline level of 385 mg/dL on July 5, 2005. He was admitted for treatment. Methadone, morphine, and STI571 were discontinued, and he was treated with IV fluids and Novolin R® (sliding scale). Levofloxacin was added later that day for a possible infection; however, blood and urine cultures came back negative, and it was discontinued on July 17, 2005. Although the patient's blood glucose level had decreased to his baseline level within 24 hours, it remained unstable (varying from 40 to 314 mg/dL) between July 15 and July 17, 2005. As a result, the patient was switched to Lantus® on July 17, 2005. The next day he was restarted on STI571, with his blood glucose level ranging from 150 to 210 mg/dL. By July 21, 2005, the site reported that the patient was more oriented and cooperative, but was still being maintained on IV fluids due to poor nutritional status.

The patient's past medical history is significant for diabetes mellitus, coronary artery disease, gastrointestinal bleed, and rheumatoid arthritis. Medications taken at the time of the event included insulin, methadone, morphine, and lorazepam.

There have been four other incidences of hyperglycemia (all considered unlikely related to STI571) and no other incidences of psychosis reported to the NCI as serious adverse events under this IND. In this case, while the hyperglycemia is considered probably related to his diabetes, a possible causal relationship to STI571 cannot be excluded. The psychosis is considered unlikely to be related to the investigational agent but due to the hyperglycemia. There have been 2365 patients enrolled in NCI-sponsored clinical trials under this IND.

	<b>Glucose, serum-high</b>	<b>Psychosis (hallucination/delusions)</b>
<b>STI571</b>	Possible	Unlikely
<b>Diabetes</b>	Probable	Possible
<b>Hyperglycemia</b>		Probable

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Date:

7/25/05

Signature:



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

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

cc: Faith Williams and Clinical Safety & Epidemiology  
Norvartis Pharmaceuticals Corporation

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