



DATE: SEP 17 2010

FROM: Pamela J. Harris, M.D., Investigational Drug Branch, CTEP, DCTD, NCI

SUBJECT: Sunitinib Malate (SU011248 L-malate; Sutent[®]) NCI IND Safety Report, AE# 1272083

TO: Investigators Using Sunitinib Malate (NSC 736511)

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 sunitinib malate.

The following must be completed by all investigators using sunitinib malate under NCI IND 74019:

- 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 74019, 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 sunitinib malate, there does not appear to be a change in the risk-benefit ratio for sunitinib malate 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 Assessments describe 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 54-year-old female with non-small cell lung carcinoma experienced a grade 5 lung hemorrhage while on a phase 3 trial utilizing the investigational agent sunitinib malate.

ADVERSE EVENTS ASSESSMENT

IND 74019 NSC 736511 Sunitinib malate (SU011248 L-malate; Sutent®)	ADVERSE EXPERIENCE REPORT NO. IND Safety Report: #1 Event: Gr. 5: Hemorrhage, pulmonary/upper respiratory: Lung
AE: 1272083	Protocol: CALGB-30607

The patient was a 54-year-old female with non-small cell lung carcinoma who died from a lung hemorrhage while on a phase 3 trial utilizing the investigational agent sunitinib malate. She began the first course of treatment on June 8, 2010, receiving sunitinib malate/placebo 37.5 mg PO daily, every 21 days. She received her last dose of sunitinib malate on June 27, 2010 (Cycle 1, Day 20).

The patient was diagnosed with non-small cell lung carcinoma in October 2009 while she was admitted for management of extensive burns from a cooking fire. She was status post multiple-agent systemic chemotherapy from February to April 2010. She began the investigational therapy with sunitinib malate on June 8, 2010.

On June 28, 2010 (Cycle 1, Day 21), the patient suddenly developed gross hemoptysis. She was brought to the emergency room in full cardio-pulmonary arrest, and resuscitative measures were initiated. Atropine and epinephrine were administered with minimal response. She continued to have hemoptysis. The patient's condition further deteriorated as she went into ventricular tachycardia, and later asystole. The resuscitation efforts were terminated, and the patient expired at 3:00 AM.

The patient's past medical and surgical history was significant for GERD, constipation, and extensive burns in October 2009. Medications taken at the time of the event included senna, Colace®, oxycodone, benzonatate, metoprolol, and famotidine.

There have been 2 other cases of lung hemorrhage and 1 case of bronchopulmonary hemorrhage reported to the NCI as serious adverse events through AdEERS under the sunitinib malate NSC and/or IND. The attributions are summarized in the following table:

Adverse Event	Grade	Attribution
Lung hemorrhage (n = 2)	3	1 Possible
	2	1 Possible
Bronchopulmonary hemorrhage (n=1)	5	1 Possible

There have been 2,657 patients enrolled in NCI-sponsored clinical trials under the sunitinib malate IND and/or NSC.

In this case, it is thought that a possible relationship exists between the adverse event and sunitinib malate.

	Lung hemorrhage
Sunitinib malate	Possible
Non-small cell lung cancer	Definite

Date: 9/16/2010

Signature:



Pamela J. Harris, M.D.
(IDB Monitor for sunitinib malate)

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

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