

North Central Cancer Treatment Group

N04C2, An Exploratory, Randomized, Placebo-Controlled Trial of Depot Octreotide (Sandostatin LAR[®] Depot) for Symptomatic Ascites in Cancer Patients

Addendum 1 – May 26, 2006

Summary

Scientific Changes:

- The schema has been corrected. Octreotide is to be administered once on day 1.
- When the patient completes treatment with the study medication, the treatment assignment may be given to the investigator.
- The consent form has been corrected. Patients are required to give ascites and blood samples for research so it is not necessary for them to agree to this separately in the consent form.

Editorial/administrative changes.

- Sandostatin LAR Depot instructions have been corrected

Replacement pages are included. Please incorporate into the protocol and keep this addendum with your protocol.

Title page: Reflects the addition of Addendum 1 and the current NCI version date.

Page 2: **Protocol Resource Page:** The following are corrections and additions to the Protocol Resource page as follows:

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Page 4: **Schema:** The schema has been corrected to reflect octreotide/placebo is to be administered once on day 1, and also included in the schema is the definition of a cycle.

Cycle = 1 month

Page 12: Section 6.16 has been corrected as follows:

6.16 Treatment cannot begin prior to registration and must begin \leq ~~24~~**48** hours after paracentesis.

Page 13: **Section 7.0 Protocol Treatment:**

The column identifying the arms has been deleted as this is a double blind study. The dose level column for the placebo for injectable solution in the treatment schedule has been corrected.

2 mL placebo microparticles/vehicle ~~30 mg normal saline~~

Section 7.11 has been corrected as follows:

Treatment with octreotide or placebo will commence no later than ~~24~~**48** hours after paracentesis. Patients will initially receive one subcutaneous injection of 100 mcg/1 mL octreotide acetate injection, or one subcutaneous injection of 1 mL 0.9% Sodium Chloride Injection.

The patient will then be assessed the following working day for toxicity, according to the criteria in section 8.0 of the protocol. If the study drug or placebo is satisfactorily tolerated, patients will then receive octreotide acetate for injectable suspension (Sandostatin LAR Depot), 30 mg IM or an IM injection of **placebo Sandostatin LAR 30 mg microparticles in a 2mL vehicle** ~~an equivalent volume of normal saline (as the placebo)~~.

Section 7.12 has been corrected:

Placebo is to be handled in a manner identical to active drug. Syringes used for administration of the active drug are to be identical to those used for administration of placebo. **The active drug is supplied in a kit which includes a syringe containing diluent. This syringe is to be used to dilute the Sandostatin LAR Depot powder and should then be discarded. A new syringe and 19 gauge, 1 1/2 " needle should be used to withdraw the subject's dose from the vial.**

Page 19: **Section 13.0 Treatment/Follow-up Decision at Evaluation of Patient:**

Section 13.4 has been corrected:

13.4 ~~If a patient does not receive treatment (and is classified as a cancel), it is necessary to provide follow up information. The patient will go directly to the event monitoring phase of the study. On-study material is to be submitted.~~ **A patient is deemed a cancel if he/she is removed from the study for any reason before any study treatment**

is given. On-study material must be submitted. No further data submission is necessary.

Section 13.5 has been added for clarification.

Patients who remain on octreotide/placebo for two years do not go on to event monitoring.

Section 13.6 has been added. Investigators may find out the treatment assignment when the patient completes treatment with octreotide/placebo.

When the patient completes treatment with octreotide/placebo, the Randomization Center may be called to find out which study therapy the patient was receiving. The patient will be told whether they received octreotide or placebo.

Page 22: **Section 15.0 Drug Information**

Section 15.21 has been corrected:

15.21 Formulation and storage: Sandostatin LAR Depot (octreotide acetate for injectable suspension) is supplied as 5 mL **vial of 30 mg octreotide acetate with a syringe containing 2.5 mL** of ~~30 mg vial with a syringe containing 2.5 mL~~ diluent. Store the product at refrigerated temperatures between 2°C - 8°C (36°F - 46°F) and protect from light during storage.

Section 15.22 has been corrected:

15.22 Preparation and Mixing: Prepare the Sandostatin LAR Depot and matching placebo as instructed on a Novartis Instruction sheet, video, or CD. These will be available on a limited basis from the NCCTG pharmacy. You can also find on-line mixing instructions at <http://www.us.sandostatin.com> or call 1-877-LAR-HELP for information on preparation. **Syringes used for administration of the active drug are to be identical to those used for administration of placebo.**

Page 28-29: In Section 18.0, the table has been revised. An evaluation is defined as monthly. The event monitoring is not submitted at the end of treatment.

Footnotes in Section 18.1 Submission Timetable have been added for clarity

1. For 2 years from on-study. **Patients who remain on octreotide/placebo for two years do not go on to event monitoring.**
2. Monthly. ~~or at time of paracentesis if therapeutic paracentesis is needed.~~ **(If a paracentesis is done during the month, it will be reported at the 1 month evaluation)**

- 3. **The 24 hour and 2 week adverse event assessment will not be submitted individually but should be recorded within the Cycle 1 (1st month) Adverse Event Log. The highest grade observed this cycle and the relationship to study medication is to be recorded when completing the Adverse Event Log."**
- 4. **The patient questionnaire booklet is submitted after the 2 week evaluation and then monthly.**

Appendix I,
Page 2 of 8

The investigator and patient may be told of the treatment assignment when the treatment portion of the study is complete. This has been added to the consent form.

At the end of treatment with the study medication, you will be told whether you were taking octreotide or the placebo

Page 6 of 8:

Since willingness to provide ascites fluid and a blood sample are required by the study, the consent form has been corrected to delete the paragraphs on Page 6 where patients are requested to initial and date their agreement to provide these samples.

~~**Please read the following statements and mark your choice:**~~

~~I agree to provide an ascites sample(s) to: NCCTG for research testing planned as part of this study.~~

~~Yes _____ No _____ Please initial here: _____
Date: _____~~

~~**For Mayo Rochester ovarian cancer patients only:**~~

~~A blood sample will be done by drawing some blood from a vein. The blood will be taken just before treatment starts.~~

~~I agree to provide a blood sample(s) to NCCTG for research testing planned as part of this study.~~

~~Yes _____ No _____ Please initial here: _____
Date: _____~~