

North Central Cancer Treatment Group

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

Update 2 – July 10, 2009

Summary

Administrative/editorial changes.

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

Title page Updated NCI version date and addition of Update 2 have been added.

Protocol Resource Page

Page 2: Roxann Neumann's contact information has been added to the table under **Non-paraffin biospecimens:**
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Section 14.0 **Translational/Pharmacologic Studies**

Page: 19-20 In order to reflect current contact information, Sections 14.1111 and 14.114 have been updated as follows:

14.1111 Kits will be supplied through **MCLCT MML**. Participating institutions may obtain kits by faxing the Supply Order Form (found in the Forms Packet) to the number listed on the form.

14.114 **MCLCT-MML** at Mayo Clinic Rochester will receive the samples and send to the Biospecimen, Accessioning, and Processing (BAP) laboratory, Stabile 13-10A, attention BAP Supervisor.

North Central Cancer Treatment Group

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

*For any communications regarding this protocol,
please call the protocol resource person on the following page.*

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Paul L. Schaefer, M.D. (NCCTG)

Study Cochairs: Lynn C. Hartmann, M.D. (Research Base)
Karin F. Giordano, M.D. (Research Base)

Laboratory: Dietrich Matern, M.D. √

Statistician: Rui Qin, Ph.D. √
507/ 538-3837

***Investigator having NCI responsibility for this protocol**

√Study contributor(s) not responsible for patient care

Document History	(Effective Date)
Activation	10/28/05
Addendum 1	May 26, 2006
Update 1	January 26, 2007
Addendum 2	July 13, 2007
Addendum 3	November 23, 2007
Addendum 4	November 21, 2008
Update 2	July 10, 2009

<u>Study Participants</u>	<u>Date Activated</u>
Entire NCCTG	October 28, 2005

NCI Version Date: June 18, 2009

Protocol Resource

	Questions:	Contact Name:
Add 1 Add 4	Patient eligibility*, test schedule, treatment delays/interruptions/adjustments, dose modifications, adverse events, forms completion and submission.	Monica Hansen NCCTG <i>Research Base</i> Quality Control Specialist Phone: 507/284-1623 Fax: 507/284-1902 E-mail: hansen.monica@mayo.edu
	Drug administration, infusion pumps, nursing guidelines	Lisa A. Kottschade, RN, MSN, CNP. NCCTG <i>Research Base</i> Nurse Phone: 507/538-7888 Mary B. Wilwerding, R.N. NCCTG Member Nurse Phone: 402/991-8070 Ext. 202
Add 4		Melissa Hogston NCCTG Member Clinical Research Associate Phone: 734/712-5176 E-mail: hogstonm@trinity-health.org
Update 1 Add 3 Add 4	Protocol document, consent form, Regulatory issues	Tracee Shevlin NCCTG <i>Research Base</i> Protocol Development Coordinator Phone: 507/538-6647 Fax: 507/284-5280 E-mail: shevlin.tracee@mayo.edu
	Adverse Events (AdEERS, MedWatch, Non-AER, AML/MDS)	Pat McNamara NCCTG <i>Research Base</i> SAE Coordinator Phone: 507/266-3028 Fax: 507/284-9628 E-mail: mcnamara.patricia@mayo.edu
Update 1	Technical problems with electronic form entry.	Barbara Warren NCCTG <i>Research Base</i> Protocol Administrative Specialist Phone: (507/284-5901) Fax: (507/538-0906) E-mail: warren.barbara@mayo.edu
Update 2	Non-paraffin biospecimens	Roxann Neumann, RN, BSN, CCRP NCCTG <i>Research Base</i> Biospecimen Resource Manager Phone: (507) 538-0602 Fax: (507) 266-0824 Email: neumann.roxann@mayo.edu

* No waivers of eligibility per NCI

- 11.2 Endpoint to be evaluated
 - 11.21 Time-to next-paracentesis after enrollment.
 - 11.22 Quality of life with Common Liver Disease Questionnaire (CLDQ).
 - 11.23 Adverse Events, as recorded with CTCAE3.0 criteria
 - 11.24 Other goals as outlined in section 2 will be addressed in a descriptive manner based on the information gathered in this protocol.

12.0 Descriptive Factors

- 12.1 Cancer type: Ovarian cancer vs. primary peritoneal cancer vs. gastrointestinal cancer vs. other.
- 12.2 Ongoing diuretic therapy anticipated: Yes vs. no.
- 12.3 Liver metastases in > 25% of the liver: Yes vs. no.

13.0 Treatment/Follow-up Decision at Evaluation of Patient

- 13.1 Therapy with octreotide or placebo will be continued as outlined in sections 7.0 and 8.0.
- 13.2 If on the second day of protocol treatment (prior to administration of depot octreotide or placebo), a patient develops grade 2 or worse diarrhea, biliary toxicity or abdominal cramping, protocol therapy will be discontinued and the patient will not receive any depot octreotide or placebo.
- 13.3 The treatment code may *not* be broken except for emergencies.
- Add 1 13.4 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
- Add 1 13.5 Patients who remain on octreotide/placebo for two years do not go on to event monitoring.
- Add 1 13.6 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 he/she received octreotide or placebo.

14.0 Translational/Pharmacologic Studies

- 14.1 Vascular Endothelial Growth Factor(VEGF)
 - 14.11 Collection of specimens
 - Add 3 14.111 **Kits are required for this study.**
 - Update 2 14.1111 Kits will be supplied through MML. Participating institutions may obtain kits by faxing the Supply Order Form (found in the Forms Packet) to the number listed on the form.
 - Add 3 14.1112 The kit contains supplies and instructions for collecting, processing, and shipping specimens.

Add 3 14.1113 Kits will be sent via FedEx® Ground at no additional cost to the participating institutions. **Allow at least two weeks to receive the kits.**

Add 3 14.1114 Kits will not be sent via rush delivery service unless the participating institution provides their own FedEx® account number or alternate billing number for express service. **NCCTG will not cover the cost for rush delivery of kits.**

14.112 **ALL** sections of the form/specimen collection labels **must** be completed.

14.113 **NOTE:** Because we are now being charged for all outgoing kits, a **small**, but sufficient, supply of the specimen collection kits should be ordered prior to patient entry.

Update 1 14.114 MML at Mayo Clinic Rochester will receive the samples and send to the
Update 2 Biospecimen, Accessioning, and Processing (BAP) laboratory, Stabile 13-10A, attention BAP Supervisor.

14.12 BAP will receive 10 cc of ascites fluid in an EDTA tube. All ascites fluid will be sent to the Immunochemical Core Laboratory. VEGF in ascites will be measured with a quantitative two-site enzyme immunoassay from R&D Systems (Minneapolis, Minnesota). The inter-assay coefficient of variation (CV) is 16.6% at 42 pg/mL.

14.2 Lysophosphatidic Acid (LPA) assay

Update 1 14.21 Blood samples will be obtained for validation of the LPA assay and will be required for all Mayo Clinic Rochester patients with ovarian cancer. Ten cc of blood will be collected in purple-top tubes that contain EDTA (plasma) and forwarded to the Biospecimen Accessioning and Processing Laboratory (BAP), Stabile 13-10A. They will be left in a refrigerator for no more than 3 hours. The blood tubes will be centrifuged at 1,750 g for 15 minutes at room temperature.

Supernatants will then be transferred to Eppendorf tubes and stored at – 70 degrees centigrade in the laboratory of Dr. Dieter Matern.

15.0 Drug Information

15.1 Sandostatin for Subcutaneous Injection Investigational Supply (SOM)

15.11 Formulation and storage: Sandostatin For Subcutaneous Injection (Octreotide Acetate Injection) is supplied as a sterile solution. Ampuls containing 100 mcg/mL octreotide (as acetate) will be provided. The ampuls should be stored at refrigerated temperatures 2°C - 8°C (36°F - 46°F) and protected from light.

Add 3 15.111 Placebo: A subcutaneous injection of 1 mL of Sodium Chloride Injection USP will be administered for the placebo dose. The saline will be obtained from the commercial drug supply at the NCCTG institution (see Section 15.3)

15.12 Preparation and Mixing: Withdraw 100 mcg (1 mL) from the ampule and inject subcutaneously.

7/10/2009

FORMS PACKET

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

- Eligibility checklist (7/13/07)
- Cancer Control Specific Forms Instructions (12/18/07)
- * Forms completion instructions
- On-study form (1/16/2006)
- Baseline adverse events/symptoms (5/11/05)
- Concurrent treatment log (2/11/05)
- Evaluation/treatment form (2/11/05)
- Adverse event log (5/11/05)
- Paracentesis data collection form (1/16/06)
- End of active treatment form (1/22/07)
- Event monitoring form (2/11/05)
- Blood specimen submission form (1/22/07)
- Baseline VEGF specimen submission form (2/11/05)
- VEGF specimen submission form (12/18/06)
- Grade 4 or 5 non-AER reportable events/hospitalization form (2/11/05)
- Booklet order form (8/22/05)
- ➔ MML Fax Supply Order Form
- Patient questionnaire booklet compliance form 1/22/07)
- Booklet (*via surface mail*)

➔ designates revised/new forms

* Forms completion instructions are available on the NCCTG web site under "Remote Data Entry Screen Instructions (Forms Completion)."

Mayo Medical Laboratories
Fax Supply Order Form – No Cover Sheet Necessary
Fax to Kit Building @ 507-538-4103

Study ID: N04C2

Investigator: _____

Order Placed By: _____ Phone #: () _____

Email: _____ Fax #: () _____

<u>Name of Kit</u>	<u># of Kits Needed</u>
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N04C2 Ascites Fluid Research	_____
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Total Kits _____

Date Needed: _____
(Please be specific)

ALLOW AT LEAST TWO WEEKS TO RECEIVE THE KITS.

NOTE: Kits will be sent via FedEx® Ground at no additional cost to the participating institutions. Kits will not be sent via rush delivery service unless the participating institution provides their own FedEx® account number or alternate billing number for express service. **The study will not cover the cost for rush delivery of kits.**

Fed Ex account number (Rush deliveries only) _____

Address (kits sent to):

Questions? Contact the Biospecimen Resource Manager listed on the Protocol Resource page of the protocol.