

North Central Cancer Treatment Group

N07C2, The Use of Wisconsin Ginseng (*panax quinquefolius*) to Improve Cancer-Related Fatigue: A Randomized, Double-Blind, Placebo-Controlled Phase III Study

Addendum 5 – January 14, 2011

**Summary**

Correction to the analogue scale has been made in the Eligibility Criteria.

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

**Title page**

Updated to reflect Addendum 5 and the current version date.

**Section 3.0**

Page 14:

**Patient Eligibility**

Section 3.12 has been corrected as follows:

Men or women with a history of cancer-related fatigue as defined by an average score  $\geq 4$  over the past 30 days on the numeric analogue scale (01 – 10) (Linear Analogue Scale Fatigue Question 1; Appendix II).

## North Central Cancer Treatment Group

**The Use of Wisconsin Ginseng (*panax quinquefolius*) to Improve Cancer-Related Fatigue:  
A Randomized, Double-Blind, Placebo-Controlled Phase III Study**

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

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**Drug Availability**

**Ginseng Board of Wisconsin: Wisconsin ginseng/placebo**

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

√Study contributor(s) not responsible for patient care.

<b>Document History</b>	<b>(Effective Date)</b>
Activation	October 10, 2008
Addendum 1	February 27, 2009
Addendum 2	June 5, 2009
Update 1	December 4, 2009
Addendum 3	August 13, 2010
Update 2	August 13, 2010
Addendum 4	December 10, 2010
Update 3	December 10, 2010
Addendum 5	January 14, 2011

<b><u>Study Participants</u></b>	<b><u>Date Activated</u></b>
Entire NCCTG	October 10, 2008

NCI Version Date: December 16, 2010

Add 5

- 3.12 Men or women with a history of cancer-related fatigue as defined by an average score  $\geq 4$  over the past 30 days on the numeric analogue scale (1 – 10) (Linear Analogue Scale Fatigue Question 1; Appendix II).
- 3.13 The presence of fatigue  $\geq 1$  month prior to randomization.
- 3.14 ECOG performance score 0, 1, 2 (located on NCCTG website <https://ncctg.mayo.edu/ncctg/forms/Non-ProtocolSpecificForms> ).
- 3.15 Histologic or cytologic proven cancer other than brain cancer or CNS lymphoma, undergoing curative intent therapy (including anti-hormonal therapies such as tamoxifen or leuprolide) or those having completed curative intent therapy who were diagnosed within the past 2 years.

**Note:** If a patient is receiving treatment for their disease such as chemotherapy, targeted therapies, immunotherapy therapy or radiation therapy then, the patient must have completed  $\geq 1$  cycle of chemotherapy, targeted therapy, or  $\geq 1$  week of radiation treatment.

- 3.16 Laboratory values obtained prior to randomization
- Hgb  $\geq 11$  (must be obtained  $\leq 30$  days; patients must not be transfused  $\leq 30$  days to meet this criterion)
  - Creatinine  $\leq 1.2$  x UNL (must be obtained  $\leq 180$  days prior to randomization)
  - AST (SGOT) or ALT (SGPT)  $\leq 1.5$  x UNL (must be obtained  $\leq 180$  days prior to randomization)
- 3.17 Negative pregnancy test done  $\leq 7$  days prior to registration, for women of childbearing potential only.
- 3.18 Ability to complete patient questionnaires alone or with assistance.
- 3.19a Controlled:
- Pain ( $\leq 4$  on Linear Analogue Scale Question 3 – Appendix II)
  - Insomnia ( $\leq 4$  on Linear Analogue Scale Question 2 – Appendix II)
- 3.19b Willingness to provide blood/saliva samples for correlative studies.

**Note:** These samples are only required for those not receiving active treatment for their disease. Active treatment is defined as chemotherapy, radiation therapy, or immunotherapy, not anti-hormone therapy such as tamoxifen, aromatase inhibitors or leuprolide.

## FORMS PACKET

N07C2, The Use of Wisconsin Ginseng (*panax quinquefolius*) to Improve Cancer-Related Fatigue: A Randomized, Double-Blind, Placebo-Controlled Phase III Study

- Contents: ✓ Eligibility Checklist *(1/14/2011)*  
Continuation Phase Eligibility Checklist *(08/13/2010)*  
\* Forms completion instructions *(10/06/2008)*  
On-study form *(1/20/2009)*  
Baseline adverse events form *(10/4/2010)*  
Baseline Concurrent Treatment Form *(7/1/2008)*  
Concurrent Treatment form *(7/1/2008)*  
Baseline Blood Specimen submission form *(9/8/2008)*  
Active Monitoring During Week 5 Blood Specimen Submission form *(9/8/2008)*  
Baseline Saliva Specimen Submission Form *(9/8/2008)*  
Week 5 Saliva Specimen Submission Form *(9/8/2008)*  
Double Blind Phase Evaluation/treatment form *(9/8/2008)*  
Optional Continuation Evaluation/treatment Form *(9/8/2008)*  
Adverse event form *(10/4/2010)*  
End of active treatment/cancel notification form *(9/18/2008)*  
Grade 4 or 5 non-AER reportable events/hospitalization form *(6/12/2008)*  
Patient Questionnaire Booklet Compliance Form *(9/8/2008)*  
Booklet order form *(10/10/2008)*  
Fax supply order form  
Reimbursement Request Form

✓ designates revised/new forms

\*Generic forms completion instructions are available on the NCCTG web site under “the CRA link in the Remote Registration and Data Entry section and are titled “Remote Data Entry Screen Instructions (Forms Completion).”

The specific forms instructions take precedence over the generic forms instructions, so it is very important to review them in addition to the generic forms instructions.

CENTRAL CANCER TREATMENT GROUP

Eligibility Checklist

1/14/2011

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**To register a patient, access the NCCTG web page at <https://ncctg.mayo.edu/training> and enter the remote registration/randomization application.**

Has the patient ever been on a prior study entered through this Registration Office?  Yes  No

If yes: Prior study number \_\_\_\_\_; prior patient study ID number \_\_\_\_\_

Registration date (date on) (mm/dd/yyyy) \_\_\_/\_\_\_/\_\_\_\_\_

Patient study ID number (provided at time of Reg/Random) \_\_\_\_\_

NCCTG member (participant sponsor) \_\_\_\_\_

NCCTG treating location \_\_\_\_\_

NCCTG treating physician \_\_\_\_\_

Institution patient number (local subject number) \_\_\_\_\_

IRB approval date (mm/dd/yyyy) \_\_\_/\_\_\_/\_\_\_\_\_

Person Completing Form:

Last Name: **(print)** \_\_\_\_\_ First Name: **(print)** \_\_\_\_\_

Phone: \_\_\_\_\_ Fax: \_\_\_\_\_ Email: \_\_\_\_\_

Patient initials (last, first, middle) \_\_\_\_\_  
(For Mayo Rochester patients, include first four letters of last name.)

Gender (check one)  Male  Female  Unknown

Date of birth (mm/dd/yyyy) \_\_\_/\_\_\_/\_\_\_\_\_

Zip code \_\_\_\_\_

Country of Residence \_\_\_\_\_

Race (check all that apply)

- White
- Black or African American
- Native Hawaiian or Other Pacific Islander
- Asian
- American Indian or Alaska Native
- Not reported: Patient refused or not available
- Unknown: Patient unsure

Method of payment (check one)

- PI (Private Insurance)
- MR (Medicare)
- MRP (Medicare and Private Insurance)
- MD (Medicaid)
- MM (Medicaid and Medicare)
- MVA (Military or Veterans Sponsored,  
Not Otherwise Specified (NOS))
- MS (Military Sponsored [including CHAMPUS & TRCARE])
- MV (Veterans Sponsored)
- SP (Self pay [no insurance])
- NP (No means of payment [no insurance])
- OTH (Other)
- UNK (Unknown)

Ethnicity (check one)

- Not Hispanic or Latino
- Hispanic or Latino
- Not reported: Refused or data not available
- Unknown: Unsure of their ethnicity

Patient study ID number \_\_\_\_\_

Eligibility Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

**Required Characteristics**

Yes No NA

≥ 18 years of age. Age = _____.	___ ___
Men or women with a history of cancer-related fatigue as defined by an average score ≥4 over the past 30 days on the numeric analogue scale (1-10) (Linear Analogue Scale Fatigue Question 1; Appendix II). Fatigue Score = _____.	___ ___
The presence of fatigue ≥1 month prior to randomization.	___ ___
ECOG performance score 0, 1, 2. PS = _____.	___ ___
Histologic or cytologic proven cancer other than brain cancer or CNS lymphoma, undergoing curative intent therapy (including anti-hormonal therapies such as tamoxifen or leuprolide) or those having completed curative intent therapy who were diagnosed within the past 2 years. <b>Note:</b> If a patient is receiving treatment for their disease such as chemotherapy, targeted therapies, immunotherapy therapy or radiation therapy then, the patient must have completed ≥1 cycle of chemotherapy, targeted therapy, or ≥1 week of radiation treatment.	___ ___
Laboratory values obtained prior to randomization.	___ ___
<ul style="list-style-type: none"> <li>Hgb ≥11 (must be obtained ≤30 days; patients must not be transfused ≤30 days to meet this criterion). Hgb date ___/___/____. Hgb = _____.</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>Creatinine ≤ 1.2 x UNL (must be obtained ≤180 days prior to randomization). Creatinine date ___/___/____. Creatinine = _____. UNL = _____.</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>AST (SGOT) or ALT (SGPT) ≤ 1.5 x UNL (must be obtained ≤180 prior to randomization). <b>Which was done?</b> ___ AST (SGOT) date ___/___/____. AST (SGOT) = _____. UNL = _____. ___ ALT (SGPT) date ___/___/____. ALT (SGPT) = _____. UNL = _____. Both → Complete AST (SGOT) and ALT (SGPT) fields above</li> </ul>	___ ___
Negative pregnancy test done ≤7 days prior to registration, for women of childbearing potential only. Not a woman of childbearing potential ( <i>check NA</i> ) vs. negative pregnancy test date ___/___/____	___ ___
Ability to complete patient questionnaires alone or with assistance.	___ ___
Controlled: <ul style="list-style-type: none"> <li>Pain (≤4 on Linear Analogue Scale Question 3 – Appendix II) Pain Score = _____</li> <li>Insomnia (≤4 on Linear Analogue Scale Question 2 – Appendix II) Insomnia Score = _____</li> </ul>	___ ___
Willingness to provide blood/saliva samples for correlative studies. <b>Note:</b> These samples are only required for those not receiving active treatment for their disease. Active treatment is defined as chemotherapy, radiation therapy, or immunotherapy, not anti-hormone therapy such as tamoxifen, aromatase inhibitors or leuprolide. If receiving active treatment for disease ( <i>check NA</i> ).	___ ___

All responses in above section must be “Yes” unless specified as “NA.”

**Contraindications**

Yes No NA

Hypersensitivity to ginseng.	___ ___
Prior use of ginseng capsules for fatigue in the past year. <b>Note:</b> Prior use of teas or drinks containing ginseng is allowed, however, patients will be asked to avoid these beverages while on the study.	___ ___
Uncontrolled hypertension on more than one occasion (diastolic blood pressure > 100, systolic > 160) measured ≤90 days prior to randomization.	___ ___
Currently using any other pharmacologic agents or nonpharmacologic interventions to specifically treat fatigue including psychostimulants, antidepressants, acupuncture, etc. <b>Note:</b> Antidepressants used to treat items other than fatigue (such as hot flashes) are allowed if the patient has been on a stable dose for ≥1 month and plans to continue for ≥1 month. Erythropoietin agents to treat anemia are allowed. Exercise is allowed.	___ ___
Known brain metastasis or primary CNS malignancy.	___ ___
Chronic systemic steroid use (including CHOP therapy or as part of any regular cancer treatment, however, steroids used as prophylaxis for nausea and vomiting are allowed). To prevent rash with Alimta, low dose dexamethasone will be allowed.	___ ___
Diabetes Type I or II (defined by being on oral hypoglycemics or insulin).	___ ___

Patient study ID number \_\_\_\_\_

**Contraindications – (continued)**

	Yes	No	NA
Psychiatric disorder such as severe depression, manic depressive disorder, obsessive compulsive disorder or schizophrenia. (Defined per medical history).	___	___	___
≤4 weeks from major surgery to randomization, including any procedure that requires general anesthetic.	___	___	___
Any of the following: <ul style="list-style-type: none"> <li>• Pregnant women</li> <li>• Nursing women</li> <li>• Women of childbearing potential who are unwilling to employ adequate contraception</li> </ul>	___	___	___
Pain requiring opioid pain medication, however, over the counter analgesics such as Tylenol or ibuprofen are allowed.	___	___	___
Use of full dose of anticoagulant therapy (Exception: 1 mg/day of Coumadin for preventing catheter clots is allowed).	___	___	___
Use of MAO inhibitors.	___	___	___
Planning to start or complete any type of cancer therapy during the 8 week, double blind, course of the study, once randomized on the study. <b>Note:</b> If not currently getting treatment, no chemotherapy agents ≤ 21 days prior to randomization. Combination treatment regimens that have components ending at different times are allowed, as long as any part of the initially started treatment continues through the double blind portion of the study.	___	___	___
Malnutrition, active infection, significant pulmonary disease and cardiovascular disease as determined by the physician, as they could impact fatigue.	___	___	___
Use of any over the counter herbal/dietary supplement marketed for fatigue or energy (for example, products containing any type of ginseng, rhodiola rosea, high doses of caffeine, guarana, or anything called an “adaptogen”).	___	___	___
Uncontrolled nausea or vomiting or any symptom that would prevent the ability to comply with daily oral ginseng/placebo treatment.	___	___	___
Uncontrolled thyroid disorder.	___	___	___
Currently receiving single agent on blinded placebo controlled treatment trials.	___	___	___

**All responses in above section must be “No.”**

Registration Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be mm/dd/yyyy.

	Yes	No	NA
A mandatory translational research component is part of this study for patients NOT receiving chemotherapy or radiation therapy. Patients not receiving chemotherapy or radiation therapy must agree to do both the saliva and the blood sampling to participate. There will be an option to select if the patient is to be registered onto this component (Section 14.0). <ul style="list-style-type: none"> <li>• Patient is receiving active treatment and will not provide blood/saliva for research testing (<i>check NA</i>).</li> <li>• Patient is not receiving active treatment and will provide blood/saliva for research testing</li> </ul>	___	___	___
Consent form signed and dated. Date of consent ___/___/____.	___	___	___
Authorization for use and disclosure of protected health information signed and dated. <b>Non-USA institution only</b> ( <i>check NA</i> ) vs. Date of authorization ___/___/____.	___	___	___
Treatment on this protocol must commence at the accruing membership under the supervision of an NCCTG member physician.	___	___	___
Treatment cannot begin prior to registration and must begin ≤30 days after randomization.	___	___	___
Pretreatment tests/procedures (see Section 4.0) must be completed within the guidelines specified in the test schedule.	___	___	___
All required baseline symptoms (see Section 10.3) must be documented and graded.	___	___	___
Study drug availability checked.	___	___	___

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Patient study ID number \_\_\_\_\_

Registration Check (*continued*)

Yes No NA

Blood draw kit and saliva collection kit availability checked. If not applicable ( <i>check NA</i> )	___	___	___
Patient questionnaire booklet availability checked; copies are not acceptable for this submission.	___	___	

**All responses in above section must be “Yes” unless specified as “NA.”**

<p><b>Is patient receiving active treatment?</b>                  ___ Yes. If yes, go to Stratification factors.                  ___ No. If no, continue with Registration questions.</p>	
<p>At the time of registration/randomization, the following will also be recorded:</p> <ul style="list-style-type: none"> <li>• Patient has given permission to keep blood sample(s) for use in future research to learn about, prevent, or treat cancer.</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>• Patient has given permission to keep blood sample(s) for use in future research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer’s disease, or heart disease).</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>• Patient has given NCCTG permission to give blood sample(s) to outside researchers.</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>• Patient has given permission to keep saliva sample(s) for use in future research to learn about, prevent, or treat cancer.</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>• Patient has given permission to keep saliva sample(s) for use in future research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer’s disease, or heart disease).</li> </ul>	___ ___
<ul style="list-style-type: none"> <li>• Patient has given NCCTG permission to give saliva sample(s) to outside researchers.</li> </ul>	___ ___

**All responses in above section may be “Yes” or “No”.**

Stratification Factors

Baseline fatigue score  
 \_\_\_ 4-7  
 \_\_\_ 8-10

Duration of all prior cancer treatment in patients lifetime  
 \_\_\_ None  
 \_\_\_ ≤180 days  
 \_\_\_ >180 days

Disease status of current cancer  
 \_\_\_ Initial diagnosis  
 \_\_\_ Recurrent disease

Current tumor type  
 \_\_\_ Hematologic  
 \_\_\_ Solid tumor malignancy

Note: Patients with both types of malignancies, select hematologic.

Current treatment (chemotherapy, radiation, immunotherapy):  
 \_\_\_ Yes  
 \_\_\_ No

Assigned Treatment

\_\_\_ Panax quinquefolius (Wisconsin ginseng) vs. Placebo

Person registering \_\_\_\_\_ Signature      Registration Office specialist \_\_\_\_\_ initials

Physician \_\_\_\_\_ Signature      M - D - Y