



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Operations Office

Date: July 25, 2008

To: Primary Clinical Research Associates

From: Tracee L. Shevlin
Research Protocol Specialist

Re: N06CA, The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

This study is reopened to patient enrollment at Mayo Clinic Rochester only, per the Status Change Notice dated July 25, 2008.

Please note that NCCTG Addendum 1 has some changes to the protocol and consent forms that only apply to Mayo Clinic Rochester. This addendum may be submitted for expedited review by your IRB, depending on your local IRB policy.

Please feel free to contact with me any questions, at 507-538-6647 or shevlin.tracee@mayo.edu.

Thank you.

North Central Cancer Treatment Group

N06CA, The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

Status Change – July 25, 2008

NOTICE OF STATUS CHANGE

This study is reopening to patient enrollment at Mayo Clinic Rochester only, effective July 25, 2008.

The accrual objective for this study has been met. However, we will accrue 9 more patients at Mayo Clinic Rochester in order to satisfy the translational goal.

Please retain this notice with the protocol.

North Central Cancer Treatment Group

N06CA, The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

Addendum 1 – July 25, 2008

Summary

- The translational component blood draw for Mayo Clinic Rochester patients only has been moved from any time between weeks 6-12 to anytime between weeks 3-4.
- Editorial/Administrative revisions

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

Title page The title page has been updated to reflect the current addendum and to replace statistician ~~Jeff Sloan, Ph.D.~~ with **Rui Qin, Ph.D.**

Protocol Resource Page

Page 2: **Melissa Hogston** replaces ~~Jeanette Lovas~~ as the NCCTG Member Clinical Research Associate. **Tracee Shevlin** replaces ~~Daniel Satele~~ as the NCCTG Research Base Protocol Development Coordinator.

Section 3.0 **Patient Eligibility**

Page 13: The pregnancy test inclusion criterion (3.19a) was removed as it conflicts with criterion 3.28 and women of childbearing potential are not eligible for enrollment. It was replaced with an additional eligibility criterion (3.19a) for the purpose of clarification.

~~3.19a Negative pregnancy test done \leq 7 days prior to registration, for women of childbearing potential only.~~

3.19a Women who are not able to bear children. Note: This is defined by those who are menopausal (12 months and no menstrual period if natural menopause), have had a hysterectomy and/or oophorectomy, permanent surgical sterilization (tubal ligation).

Section 4.0 **Test Schedule**

Page 15: The time-point for the research blood draw (for Mayo Rochester patients only) has been moved to the double-blind phase of the study. The corresponding

footnote has been revised to state the blood draw should occur sometime during weeks 3 or 4 rather than 5-12.

Section 6.0

Page 18:

Registration/Randomization Procedures

Section 6.24 was moved to section 6.13 and subsequent sections were renumbered accordingly. This section refers to the translational component of the study which is now being conducted in the double blind phase (i.e. as part of section 6.1) rather than during the continuation phase (i.e. part of section 6.2)

Section 7.0

Page 19:

Protocol Treatment

The reference to section 14.0 for the translational component of the study was moved from section 7.3 (continuation phase treatment) to section 7.1 (double-blind phase treatment).

Section 14.0

Pages 25-27

Non-solid Tissue (Body Fluid) Biospecimens

All references in this section to the continuation phase and weeks 6-12 have been revised to reflect the blood being drawn during the double-blind phase weeks 3 or 4.

Section 15.0

Page 27

Drug Information

This study required an IND and thus the reference to ~~IND-exempt~~ has been deleted and replaced with **IND 78,250**.

Section 16.0

Page 32

Statistical Considerations

Section 16.329 has been revised as follows to coincide with the revision of the blood draw time point.

16.329 Related to goal 2.23: Because participation in the translational component is expected to be small (since it is limited to patients at Mayo Rochester ~~on the continuation phase and further is optional~~), the investigation of systemic absorption is exploratory. ~~Since the blood draw occurs during the continuation phase, all patients will have received (at least two weeks worth of in most cases) the active agent.~~ The proportion of patients with any detectable (i.e., non-zero) level will be computed for each of the three components of the gel (amitriptyline HCl, baclofen, and ketamine/norketamine). **The patients on placebo will be compared with patients on active agent, descriptively. Since the sample sizes are likely to be no larger than 5 each, we are only looking for evidence of systemic absorption in a descriptive manner, not looking for statistically significant differences between groups in any way. Further analysis will depend on the amount of data received, but may include a comparison of the proportions between the original treatment arm assignments using Fisher's Exact test.**

Section 18.0 **Records and Data Collection Procedures**

Page 36

The table in section 18.1 has been revised to allow initial materials to be entered ≤ 4 weeks after registration rather than ≤ 2 weeks since patients are allowed 28 days following registration to begin treatment.

Footnote 8 has been revised to state that blood will be collected at any time during weeks 3-4 rather than 6-12.

Consent Form

Page 6:

The biological specimens portion of the consent has been revised as follows to reflect the updated blood draw schedule.

During the first part of the study (the first 4 weeks) when you are receiving either placebo or the active gel, you will be asked to participate in a ~~There will be an additional 8 week continuation phase of the study which includes a laboratory test that will use a small sample of blood. If you decide to continue or start the BAK gel (if you were using the placebo) for the additional 8 week continuation phase of the study, a~~ **A blood sample will be done by drawing some blood (3 Tbsp or 40 ml) from a vein. The blood will be taken one time during weeks 2 through 8 of this 8 week continuation phase** ~~3 or 4 of the study.~~

North Central Cancer Treatment Group

The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

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

Study Chairs: Debra L. Barton, RN, PhD, AOCN (Research Base)
Mayo Clinic
200 First Street, SW
Rochester, MN 55905
507/284-1623
507/284-5280 (FAX)
barton.debra@mayo.edu

Edward Wos, MD (NCCTG)

Study Cochairs: Charles L. Loprinzi, MD (Research Base)*
Sherry L. Wolf, RN, MS (Research Base)

Statistician: Rui Qin, PhD ✓
(507) 266-2380

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

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

Document History	(Effective Date)
Activation	Feb 22 2008
Addendum 1	July 25, 2008

<u>Study Participants</u>	<u>Date Activated</u>
Entire NCCTG	Feb 22 2008

NCI Version Date: June 25, 2008

Protocol Resources

Questions:	Contact Name:
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 Kottschade, RN, MSN, CNP NCCTG <i>Research Base</i> Nurse Phone: (507) 538-7888 E-mail: kottschade.lisa@mayo.edu Mary Collins, RN, MSN, OCN NCCTG Member Nurse Phone: (217) 383-6847 E-mail: mary.collins@carle.com
Forms completion and submission	Melissa Hogston NCCTG Member Clinical Research Associate Phone: 734-712-5176 Email: hogstonm@trinity-health.org
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)	Patricia G. McNamara NCCTG <i>Research Base</i> SAE Coordinator Phone: (507) 266-3028 Fax: (507) 284-9628 E-mail: mcnamara.patricia@mayo.edu
Technical problems with electronic form entry	Brandon Messmer NCCTG <i>Research Base</i> Data Management Specialist Phone: (507) 538-4633 Fax: (507) 538-0906 E-mail: messmer.brandon@mayo.edu

*No waivers of eligibility per NCI

vincristine or vinblastine, or other neurotoxic chemotherapy agents such as bortezomib, lenalidomide or thalidomide). Note: Patients on daily chemotherapy will not be eligible for this trial.

- 3.12 Pain or symptoms of peripheral neuropathy of duration ≥ 1 month attributed to chemotherapy.
- 3.13. A score of ≥ 4 out of 10 on the numbness/tingling/pain numeric analogue scale (see Appendix VII).
- 3.14 ≥ 18 years of age.
- 3.15 Ability to sign informed consent and understand the nature of a placebo-controlled trial.
- 3.16 ECOG Performance Status (PS) of 0, 1, or 2. (This form is now on the NCCTG website <https://ncctg.mayo.edu/ncctg/formsNonProtocolSpecificForms/>.)
- 3.17 Ability to complete questionnaires by themselves or with assistance.
- 3.18 Life expectancy ≥ 4 months.
- 3.19a Women who are not able to bear children. Note: This is defined by those who are menopausal (12 months and no menstrual period if natural menopause), have had a hysterectomy and/or oophorectomy, permanent surgical sterilization (tubal ligation).
- 3.19b Creatinine ≤ 1.5 X UNL obtained ≤ 90 days prior to registration.
- 3.19c Neuropathy limited to either hands or feet (or both) where gel can be applied.

3.2 Contraindications

- 3.21 Pre-existing or history of peripheral neuropathy due to any cause other than chemotherapy (diabetes, alcohol, toxin, hereditary, etc.).
- 3.22 History of an allergic reaction to amitriptyline HCl, baclofen, and/or ketamine.
- 3.23 Treatment ≤ 30 days with anticonvulsants, tricyclic antidepressants, MAO inhibitor, or other neuropathic pain medication agents such as carbamazepine, phenytoin, valproic acid, gabapentin, lamotrigine, topical lidocaine patch or gel, capsaicin cream, amifostine, etc.

Note: Patients who have taken any of these agents for peripheral neuropathy for ≤ 1 week during the past 30 days, but are no longer taking the agent, are not excluded.

- 3.24 Diagnosis of coronary artery disease including but not limited to MI, PTCA, or CABG ≤ 5 years or diagnosis of congestive heart failure of any NY heart class I-IV (this form is now on the NCCTG website <https://ncctg.mayo.edu/ncctg/formsNonProtocolSpecificForms/>). Note: Valve

4.0 Test Schedule

Tests and procedures	Active-Monitoring Phase			
	Double-Blind Phase			Optional Continuation Phase
	≤30 days prior to registration	Baseline	Weekly x 4 weeks (weeks 1-4)	Weekly x 8 weeks (weeks 5-12)
History and exam, weight, performance status, including mental status exam and skin examination of hands and feet ²	X			
Creatinine Blood Test	X ¹			
Peripheral Neuropathy Question (Appendix VII)	X ¹¹			
Patient questionnaire booklet completion ³ EORTC QLQ-CIPN20 (Appendix III) ¹⁰ BPI (Appendix V) ¹⁰ POMS-B (Appendix IV) ¹⁰ Symptom Experience Diary (Appendix II) Peripheral Neuropathy Question (Appendix VII) Subject Global Impression of Change (Appendix VI) ⁸		X	X	X ^{6,7}
Adverse Event Assessment ^{4,5}		X	X	X ⁶
Research Blood Draw (MCR Participants ONLY)			X ^R	
CRA/Nurse phone call ¹² (Appendices VIII and IX), Neurotoxicity Evaluation (Appendix XI)		X ⁹	X ⁵	X ^{5,6}

1. Must be obtained ≤ 90 days prior to registration and is considered standard treatment to evaluate renal function.
2. Skin assessment of hands and feet must be done ≤7 days prior to registration.
3. Patient questionnaire booklets **must** be used and completed weekly; copies are not acceptable for this submission. A self-addressed, stamped envelope will be provided for patients to return questionnaires to the healthcare provider and/or study staff.
4. May be completed over the phone or at in-person visit. When the patient is seen in the clinic, health care personnel are to (in person) evaluate skin integrity of hands and feet as well as mental status using the CTC.
5. On weeks when the patient is not seen in the clinic, the CRA/Nurse phone call is used to evaluate compliance and adverse events, answer questions, and encourage questionnaire completion and return.
6. Continuation on the study can only occur after the treatment site has received completed patient questionnaires from the double-blind phase of the study.
7. Appendices II (SED) and VII (Peripheral Neuropathy Question) to be completed weekly during weeks 5-12. Appendix III (EORTC QLQ-CIPN20) to be completed at weeks 6, 8, 10, and 12. Appendix IV (POMS-B) to be completed at weeks 8 and 12. Appendix V (BPI) does not need to be completed during the continuation phase.
8. To be completed at the end of week 4 only (i.e., before unblinding occurs).
9. For the Provider Rated Peripheral Neuropathy Scale (CTC) only.

After the patient has been registered into the study, the values of the stratification factors (Section 5.0) will be recorded, and the patient will be randomly assigned to one of the following treatment groups:

- Topical gel of amitriptyline HCl, baclofen, and ketamine bid
- Identical placebo gel bid

6.13 Translational Research (Mayo Clinic Rochester patients only)

An optional translational research component is part of the study for Mayo Clinic Rochester patients only. There will be an option to select if the patient is to be registered onto this component (Section 14.0).

- Patient has/has not given permission to give a blood sample for research testing.

6.14 Procedures for Double-Blinding the Treatment Assignment

6.141 After the treatment assignment has been ascertained by the remote registration/randomization application, the patient's study medication code number will be displayed on the confirmation of registration screen.

6.1411 The data manager/nurse/pharmacist at the patient's institution must contact the randomization center for a code number when additional study product is needed for the patient.

6.142 The number of the treatment assigned to the patient will be recorded on the dosing form.

6.143 Randomization Center personnel will monitor the supply of coded bottles at each participating institution and will arrange for the Research Base oncology pharmacist to send further supplies to the participating institutions as needed.

6.2 Optional Continuation Study

6.21 The double-blind phase of the study must be completed prior to the treatment code being broken; that is, after the treating site has received the completed patient questionnaire booklet.

6.22 If the patient and physician want to continue with the active gel, or if on placebo, begin the active gel, call (507/284-4130) or fax (507/284-0885) a completed continuation phase eligibility checklist to the Randomization Center between 8 a.m. and 4:30 p.m. central time Monday through Friday.

6.23 Treatment cannot begin prior to registration and must begin ≤ 28 days after registration.

7.0 Protocol Treatment

7.1 Treatment Schedule

Agent	Dose Level	Route	Day	Duration of Treatment
Amitriptyline HCl/ ketamine/baclofen gel	1.31 grams of compounded gel = 40 mg amitriptyline HCl, 10 mg baclofen, 20 mg ketamine. Contents of one level measuring spoon which will be supplied.	Apply one level spoonful of gel topically to <u>each area</u> of pain, numbness, and/or tingling ¹	Twice daily (in morning and before bedtime)	4 weeks; study gel will not be applied on days patients are receiving chemotherapy treatment
Placebo gel	1.31 grams of gel = Contents of one level measuring spoon which will be supplied	Apply one level spoonful of gel topically to <u>each area</u> of pain, numbness, and/or tingling ¹	Twice daily (in morning and before bedtime)	4 weeks; study gel will not be applied on days patients are receiving chemotherapy treatment

1. No more than 4 areas of pain, numbness, and/or tingling should be treated at a single time point (i.e. max 4 spoonfuls of gel per application).

See Appendix X for Patient Instructions for Pain/Placebo Gel Application.

Refer to 14.0 if a Mayo Rochester patient is participating in optional blood draw.

- 7.2 In the event of an emergency, call the Randomization Center at (507) 284-4130 to break the code on Monday through Friday, 8:00 a.m. to 4:30 p.m. central time.

7.3 Optional Continuation Phase

Agent	Dose Level	Route	Day	Duration of Treatment
Amitriptyline HCl/ ketamine/baclofen gel	1.3 grams of compounded gel = 40 mg amitriptyline HCl, 10 mg baclofen, 20 mg ketamine. Contents of one level measuring spoon which will be supplied.	Apply one level spoonful of gel topically to <u>each area</u> of pain, numbness, and/or tingling ¹	Twice daily (in morning and before bedtime)	8 weeks

1. No more than 4 areas of pain, numbness, and/or tingling should be treated at a single time point (i.e. max 4 spoonfuls of gel per application).

Participants may choose to continue on the active gel or if on placebo, begin the active gel for an additional 8 weeks. Participants may not start on the continuation phase of the study until questionnaire data from the double-blind phase has been received by the

13.0 Treatment/Follow-up Decision at Evaluation of Patient

13.1 A patient is deemed *ineligible* if, at the time of registration, the patient did not satisfy each and every eligibility criteria for study entry.

- If the patient received treatment, all data up until the point of confirmation of ineligibility must be submitted and patient should be taken off study.
- If the patient never received treatment, initial material must be submitted.

The patient may continue non protocol treatment at the discretion of the physician as long as there are no safety concerns, and the patient was properly registered.

13.2 A patient is deemed a *major violation*, if protocol requirements regarding treatment in cycle 1 of the initial therapy are severely violated that evaluability for primary end point is questionable. All data up until the point of confirmation of a major violation must be submitted. The patient may continue non-protocol treatment at the discretion of the healthcare provider as long as there are no safety concerns, and the patient was properly registered.

13.3 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 and the End of Active Treatment/Cancel Notification Form must be submitted.

13.4 During the double-blind phase of the study, if, in the judgment of the attending physician or allied health professional, it would be helpful for the future clinical care of the individual patient, the code may be broken. The Randomization Center may be called to find out which study therapy the patient was receiving. Participants may choose to continue on the active gel or if on placebo, begin the active gel for an additional 8 weeks. Assessments of efficacy per the EORTC QLQ-CIPN20 (Appendix III), Peripheral Neuropathy Question (Appendix VII), and side effects per the Symptom Experience Diary (Appendix II) will be collected. The POMS-B (Appendix IV) will be assessed at weeks 4 and 8 of the continuation phase. Participants may NOT receive gel and start on the continuation phase until questionnaire data has been received by the treatment site.

14.0 Non-solid Tissue (Body Fluid) Biospecimens

14.1 Non-solid Tissue Biospecimen Submission – **MAYO CLINIC ROCHESTER (MCR) PARTICIPANTS ONLY.**

NOTE: Participants must have consented to submission of the following tissue(s).

Type of biospecimen to submit	Mandatory or optional	When to submit ¹	Reason for submission (background/methodology section)	Where to find specific details for specimen submission
Blood/blood products (serum and plasma)	Optional MCR participants ONLY	One time during weeks 3 or 4.	Determination of study drug concentrations (Section 14.4)	Section 14.2

¹**Draws must be collected within 8 hours of last gel application.**

14.2 Blood/Blood Products

14.21 **Kits are not required for this study.**

14.22 All specimens must be collected and processed **Monday-Friday ONLY.**

14.23 Verify ALL sections of the NCCTG Blood Specimen Submission Form are completed and filled in correctly. Enter information from the NCCTG Blood Specimen Submission Form into the remote data entry system within 7 days of specimen collection (see Forms Packet).

14.24 Provide the participant with a pink card and direct the participant to have their blood drawn at any MCR phlebotomy laboratory.

14.25 The phlebotomy laboratory will collect blood/blood products in the order listed in the table that follows and forward the specimens and pink card to Special Study Processing (Laboratory Medicine and Pathology Department, Hilton CL) for processing.

Summary Table of Research Blood/Blood Products to Be Collected for This Protocol

Indicate if specimen is mandatory or optional	Collection tube description and/or additive (color of tube top)	Volume to collect per tube (number of tubes to be collected)	Blood product being processed	One time during weeks 3 or 4 ¹	Process at site?
Optional	None (red)	10 mL (3)	Serum	X	Yes
Optional	EDTA (purple)	10 mL (1)	Plasma	X	Yes

Blood draw must be within 8 hours of last gel application.

14.26 Special Study Processing will process the whole blood in no additive (red-top) tubes into serum and the whole blood in EDTA (purple-top) tube into plasma per standard institution protocols.

14.261 Special Study Processing will forward 3.0 mL EDTA plasma to the Drug Laboratory (Hilton 7) to determine amitriptyline HCl concentrations, test code #8125.

14.262 Special Study Processing will forward 3.0 mL serum to the Drug Laboratory (Hilton 7) to determine baclofen concentrations, test code #81255.

14.263 Special Study Processing will forward 6.0 mL serum to National Medical Services to determine ketamine/norketamine concentrations, test code #90366.

14.27 Residual serum and plasma specimens will be discarded.

14.3 Other Body Fluids (None)

14.4 Background/Methodology Information

14.41 Blood/blood product samples will be collected for the following research:

14.411 Blood will be collected one time during weeks 3-4 of the double-blind phase (draw must be within 8 hours of last gel application) to determine if this combination and dose of three opioids is absorbed systemically.

14.4111 Amitriptyline HCl levels will be measured by reverse phase high performance liquid chromatography (HPLC) in the Drug Lab at Mayo Clinic Rochester (test code #8125).

14.4112 Ketamine and norketamine will be measured by liquid chromatography/mass spectrometry at National Medical Services (test code #90366).

14.4113 Baclofen concentrations will also be measured by HPLC in the Drug Lab at Mayo Clinic Rochester (test code #81255).

14.5 Return of Genetic Testing Research Results

No genetic specimens will be collected from non-solid tissue (body fluid) biospecimens for this study.

15.0 Drug Information

- IND 78,250

15.1 Amitriptyline HCl, baclofen, and ketamine gel and matching placebo gel

15.11 Preparation and storage: An amitriptyline HCl/baclofen/ketamine PLO based gel will be compounded for use in this trial. The gel will contain the following:

Amitriptyline HCl (3.05%)

Baclofen (0.77%)

Ketamine (1.53%)

Pluronic lecithin organogel (PLO) 30%

One level spoonful contains 1.31 grams of the gel and will provide 40 mg amitriptyline HCl, 10 mg baclofen, and 20 mg ketamine.

The gel will be compounded at Gateway Compounding Pharmacy in Bismarck, North Dakota. The gel will be in wide mouthed jars and will be stored at room temperature, 59 to 86°F. The product beyond-use date will be a maximum of 6 months.

Calculations for the formulation and dose of the gel were computed by the expert compounding pharmacist at Gateway Compounding Pharmacy. The baclofen and ketamine were converted to base formulations and amitriptyline HCl will

arms using a single two-sample independent samples *t*-test or Wilcoxon rank sum test as appropriate. Also for each symptom, incidence rates (score ≥ 1) at baseline and during weeks 1-4 will be compared between the treatment arms using Fisher's exact tests.

- 16.327 Correlational analyses will be done using primary and secondary endpoints to determine the relationships between various endpoints such as CTCAE v3.0 sensory neuropathy grades and EORTC QLQ-CIPN20 sensory neuropathy scale scores. Such correlations will be done at single data points such as baseline and weeks 1 to 4.
- 16.328 The Subject Global Impression of Change Scale data will be summarized via relative frequencies of responses by treatment arm and compared between treatment arms using chi-squared testing. An anchor-based analysis similar to that present by Osoba et al.⁸⁵ will be performed using the Subject Global Impression of Change items with the EORTC QLQ-CIPN20 and the Peripheral Neuropathy Question. In particular, the Spearman rank correlations will be computed between change from baseline subscale scores (at week 4) of the EORTC QLQ-CIPN20 and the Peripheral Neuropathy Question and the scores of the Subject Global Impression of Change items. Further, the small ("a little"), moderate ("moderately"), and large ("very much") effect sizes will be computed for each subscale using the appropriate (i.e., matching) Subject Global Impression of Change item. The effect size will be computed as the mean change from baseline subscale score at week 4 divided by the standard deviation of the subscale scores at baseline.

The appropriate 95% confidence interval for the proportion of patients by treatment arm identifying the actual treatment received will be computed. If the confidence interval does not contain 50% (the percentage expected if all patients are randomly guessing), it will be concluded that the blinding was ineffective. The proportion of patients on each treatment arm continuing onto the continuation phase will also be computed.

Data from the continuation phase will be descriptively presented including summary statistics (N, mean, standard deviation, median, quartiles, and range) and plots of average scores and individual patient scores over time for each endpoint (summary statistics and plots for all patients participating on the continuation phase together and separately by original treatment arm assignment).

- 16.329 Related to goal 2.23: Because participation in the translational component is expected to be small (since it is limited to patients at Mayo Rochester), the investigation of systemic absorption is exploratory. The proportion of patients with any detectable (i.e., non-zero) level will be computed for each of the three components of the gel (amitriptyline HCl, baclofen, and ketamine/norketamine). The patients on placebo will be compared with patients on active agent, descriptively. Since the sample sizes are likely to be no larger than 5 each, we are only looking for evidence of systemic absorption in a descriptive manner, not looking for statistically significant differences between groups in any way.

18.0 Records and Data Collection Procedures

18.1 Submission Timetable

Forms	Active-Monitoring Phase (Compliance with Test Schedule)			At each occurrence	
	Initial Material	Follow-up Material		Grade 4 or 5 Non-AER Reportable Events/ Hospitalization	ADR/AER
	≤4 weeks after registration	At each evaluation (Weekly)	At end of treatment		
On-Study Form	X				
Baseline Adverse Events Form	X				
Concurrent Treatment Form	X	X	X		
Evaluation/Treatment Form ³		X	X		
End of Active Treatment/Cancel Notification Form	X ¹		X ⁶		
Adverse Event Log		X	X		
NCCTG Blood Specimen Submission Form (Section 14.0) (Mayo Rochester patients only)		X ⁸			
Patient Questionnaire Booklet ² (Appendices II through VII)	X ⁵	X ⁵	X ⁷		
Patient Questionnaire Booklet Compliance Form ⁴	X	X	X		
ADR/AER (see Section 10.0)					X
Grade 4 or 5 Non-AER Reportable Events/ Hospitalization Form				X	

1. Submit this form only if withdrawal/refusal prior to beginning protocol therapy occurs.
2. Patient questionnaire booklets **must** be used; copies are not acceptable for this submission.
3. The CRA/Nurse Worksheets (Appendix VIII and IX) as well as Appendix XI can be used as guides when making phone calls to assist in completing this form. Any comments pertinent to the evaluation of the study should be recorded in the comments section of the form.
4. This form must be completed **only** if the Patient Questionnaire Booklet contains absolutely **NO** patient provided assessment information.
5. Appendices III, IV and V to be completed at baseline and Week 4 of the double-blind phase. Appendix VI to be completed at week 4 only (i.e., before unblinding occurs). Appendices II and VII to be completed at baseline and weekly during the double blind phase.
6. Submit after 4 weeks if patient does not go on continuation phase. If patient goes on continuation phase, submit after 12 weeks. Form is completed only one time.
7. If patient goes on continuation phase, Appendices II and VII need to be completed weekly for weeks 5-12. Appendix III to be completed at weeks 6, 8, 10, and 12 only. Appendix IV to be completed at weeks 8 and 12 of the continuation phase. Appendix V does not need to be completed for the continuation phase.
8. Blood will be collected one time during weeks 3-4 for Mayo Rochester patients only.

19.0 Budget

19.1 Costs charged to patient: routine clinical care.

NCI Informed Consent Template for Cancer Treatment Trials (English Language)

*NOTES FOR LOCAL INVESTIGATORS:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices. The informed consent form provides a summary of the clinical study and the individual's rights as a research participant. It serves as a starting point for the necessary exchange of information between the investigator and potential research participant. This template for the informed consent form is only one part of the larger process of informed consent. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is <http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/>
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- Suggestion for Local Investigators: An NCI pamphlet explaining clinical trials is available for your patients. The pamphlet is entitled: "If You Have Cancer... What You Should Know about Clinical Trials". This pamphlet may be ordered on the NCI Web site at <https://cissecure.nci.nih.gov/ncipubs/> or call 1-800-4-CANCER (1-800-422-6237) to request a free copy.
- Optional feature for Local Investigators: Reference and attach drug sheets, pharmaceutical information for the public, or other material on risks. Check with your local IRB regarding review of additional materials.

*These notes for investigators are instructional and should not be included in the informed consent form given to the prospective research participant.

N06CA, The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

This is an important form. Please read it carefully. It tells you what you need to know about this research study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

This is a clinical trial, a type of research study. Your healthcare provider will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your healthcare provider for more explanation.

You are being asked to take part in this research study because you have taken or are taking a type of chemotherapy that is causing you to have peripheral neuropathy. Peripheral neuropathy is an injury to the nerves that supply sensation to the arms and legs. Some symptoms you might be experiencing may include tingling, numbness, shooting, burning, or cramping sensations in your fingers and toes.

Why is this research study being done?

The purpose of this research study is to:

- See if using BAK gel rubbed into the skin will improve symptoms of peripheral neuropathy caused by chemotherapy.
- See how the use of BAK gel affects your body, mood, pain, and quality of life.
- See the effects (good or bad) of using BAK gel.

BAK represents three medications that may be useful in relieving tingling, numbness and/or pain in your hands and feet as a result of chemotherapy. B stands for baclofen which is a muscle relaxant. A stands for amitriptyline HCl which is an antidepressant often used for nerve related pain. K stands for ketamine which is an anesthetic which is thought to relieve nerve related pain when rubbed into the skin.

How many people will take part in the research study?

About 148 people will take part in this study.

What will happen if I take part in this research study?

Before you begin the study you will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your healthcare provider.

- Medical history (you will be asked to rate your pain and any problem with numbness, tingling or pain in your fingers and/or toes)
- Physical examination
- Routine blood test to check your kidney function.

You will be "randomized" into one of the study groups to receive either medication in a Pluronic Lecithin Organogel (PLO) or plain Pluronic Lecithin Organogel (PLO) described below. PLO is type of gel designed to serve as a base gel to which medicines can be added when they are to be used on the skin. Randomization means that you are put into a group by chance (as in the flip of a coin). A computer program will place you in one of the study groups. Neither you nor your healthcare provider can choose the group you will be in. You will not be told if you are using the active gel or the placebo. You will have an equal chance of being placed in either group.

If you are in group 1 You will apply the BAK gel to the skin in the area where you are experiencing pain, tingling, or other effects from your peripheral neuropathy twice a day (in the morning and before bedtime) for 4 weeks.

If you are in group 2 You will apply the placebo gel to the skin in the area where you are experiencing pain, tingling, or other effects from your peripheral neuropathy twice a day (in the morning and before bedtime) for 4 weeks. A placebo is an inactive gel used to compare the study results with the gel listed above.

You will also be asked to complete some study questionnaires before you begin to use the gel and then each week for 4 weeks after you start using the gel. The questions will ask you about your health, mood, pain, and quality of life. You will be given a questionnaire booklet to take home with you. These questionnaires should take you approximately 30 minutes to complete.

A nurse or research assistant will also call you weekly (during the weeks you do not see your healthcare provider) to ask you about any side effects you might have from the gel and to see if you have any questions about the study or the questionnaires you are completing.

How long will I be in the research study?

You will be asked to use the gel for 4 weeks. After you are finished with the 4 weeks of the study, you will find out if you were using the BAK gel or the placebo gel. You may choose to enter a continuation phase of the study and start using the BAK gel if you were on the placebo gel (or continue using it) for an extra 8 weeks. If you decide to start or continue the BAK gel after the first 4 weeks of the study, a member of the study team will call you weekly for 8 weeks and you will also be asked to complete weekly questionnaires similar to those you completed during the first 4 study weeks.

Can I stop being in the research study?

Yes. You can decide to stop at any time. Tell your healthcare provider if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell your healthcare provider if you are thinking about stopping so any risks from the BAK gel can be evaluated by your healthcare provider. Another reason to tell your healthcare provider that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The healthcare provider may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the research study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. Since the medications in this study are not being given in their usual form (by mouth or through a shot), healthcare professionals don't know whether or not side effects may happen. In previous studies, side effects from using these drugs on the skin (topically) have been none to minimal. Side effects may be mild or very serious. Your healthcare team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the BAK gel. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your healthcare provider about any side effects that you have while taking part in the study.

More Likely Risks (when ketamine and amitriptyline have been mixed together and used topically):

- Drowsiness
- Dizziness
- Dry mouth
- Burning skin irritation, peeling, or rash at site of application
- Occasional increased heart rate
- Ringing in the ears
- Facial acne

Less Likely Risks (Seen with oral baclofen) and may occur if baclofen is absorbed into your system:

- Drowsiness
- Dizziness
- Weakness
- Fatigue
- Confusion
- Nausea (feeling sick to your stomach)
- Low blood pressure
- Constipation

- Increased need to urinate
- Inability to sleep
- Headache

Rare but serious Risks:

- Allergic reaction for any of the medications
- Hallucinations or seizures when stopping oral baclofen

Reproductive risks: Pregnant women or those that can become pregnant are not eligible of this study. Women should not breastfeed a baby while on this study.

The risks of drawing blood include pain, bruising, or rarely, infection at the needle site.

For more information about risks and side effects, ask your healthcare provider.

Are there benefits to taking part in the research study?

Taking part in this study may or may not make your health better. While doctors hope the BAK gel will be useful against peripheral neuropathy, there is no proof of this yet. We do know that the information from this study will help doctors learn more about BAK gel as a treatment for chemotherapy-induced peripheral neuropathy. This information could help future cancer patients.

What other choices do I have if I do not take part in this research study?

You do not have to be in this study to receive treatment for your peripheral neuropathy.

Your other choices may include:

- Getting treatment or care for your peripheral neuropathy without being in a study
- Taking part in another study
- Getting no treatment

Talk to your healthcare provider about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- North Central Cancer Treatment Group (NCCTG) researchers

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

[Note to Local Investigators: The NCI has recommended that HIPAA regulations be addressed by the local institution. The regulations may or may not be included in the informed consent form depending on local institutional policy.]

What are the costs of taking part in this research study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The study agent, BAK or placebo gel, will be provided free of charge while you are taking part in this study.

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage> . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this research study?

It is important that you tell your healthcare provider, _____ *[investigator's name(s)]*, if you feel that you have been injured because of taking part in this study. You can tell the healthcare provider in person or call him/her at _____ *[telephone number]*.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this research study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the research study?

You can talk to your healthcare provider about any questions or concerns you have about this study. Contact your healthcare provider _____ [name(s)] at _____ [telephone number].

For questions about your rights while taking part in this study, call the _____ [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at _____ (telephone number).
[Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]

The following section regarding biological samples for research should only be used to consent patients enrolled at Mayo Clinic Rochester

Please note: This section of the informed consent form is about an additional research study that is being done with people who are taking part in the main study. You may take part in this additional study if you want to. You can still be a part of the main study even if you say 'no' to taking part in this additional study.

You can say "yes" or "no" to the following study. Please mark your choice for the study.

About Using Biological Samples for Research

During the first part of the study (the first 4 weeks) when you are receiving either placebo or the active gel, you will be asked to participate in a laboratory test that will use a small sample of blood. A blood sample will be done by drawing some blood (3 Tbsp or 40 ml) from a vein. The blood will be taken one time during weeks 3 or 4 of the study.

The blood samples will be sent to laboratories associated with the Mayo Clinic, Rochester, where the test will be done. The test will be done in order to understand how the gel is absorbed into your body. The results of the test will not be sent to you or your healthcare provider and will not be used in planning your care. This test is for research purposes only and you will not have to pay for it. Your samples will be used as described for this study. When the study is done, they will be destroyed.

You can take part in the treatment portion of this study without taking part in this research laboratory test.

Please read the following statements and mark your choice:

1. I agree to provide a blood sample to laboratories associated with Mayo Clinic Rochester for research testing planned as part of this study.

Yes No Please initial here: _____ Date: _____

Benefits

The benefits of research using blood include learning more about how these medications are absorbed through your skin. You will also learn whether the medications in the BAK gel are being absorbed into your blood stream or whether they are staying at local sites in your hands and feet.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this form. If you want more information about this study, ask your healthcare provider.

Signature

I have been given a copy of all _____ [insert total of number of pages] pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Printed Participant Name: _____

Participant Signature: _____

Date: _____

Printed name of person obtaining informed consent:

Signature of person obtaining informed consent:

Date _____

This model informed consent form has been reviewed by DCP/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. Sections “What are the risks of the research study” or “What other choices do I have if I don’t take part in this research study?” should always be used in their entirety if possible. Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to these sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language and justification must be forwarded to the North Central Cancer Treatment Group Operations Office for approval before a patient may be registered to this study.

Consent forms will have to be modified for each institution as it relates to where information may be obtained on the conduct of the study or research subject. This information should be specific for each institution.

July 25, 2008

FORMS PACKET

N06CA, The Use of Topical Baclofen, Amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

- Contents:
- ✓ Eligibility checklist (7/25/2008)
 - ✓ Continuation phase eligibility checklist (7/25/2008)
 - On-study form (4/8/2008)
 - Baseline adverse events form (9/10/2007)
 - Adverse event form (9/10/2007)
 - Concurrent treatment form (baseline) (9/10/2007)
 - Concurrent treatment form (active monitoring phase) (2/8/2008)
 - Evaluation/treatment form (2/8/2008)
 - End of active treatment/cancel notification form (2/12/2008)
 - ✓ Continuation Phase Rochester Patients Only Optional Collection Blood Specimen Submission Form (7/15/2008)
 - Patient Questionnaire Booklet Compliance Form (2/12/2008)
 - Grade 4 or 5 non-AER reportable events/hospitalization form (1/30/2008)
 - Booklet order form (2/22/2008)
 - * N06CA forms completion instructions (2/14/2008)

✓ Designates new/revised form.

*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.

NORTH CENTRAL CANCER TREATMENT GROUP
N06CA Eligibility Checklist

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N06CA: The Use of Topical Baclofen, amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

This study is open to RMC Patients only. 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/Allied health professional _____

Institution patient number (local subject number) _____

IRB approval date (mm/dd/yyyy) ___/___/_____

Patients initials (last, first, middle) _____
(For Mayo Rochester patients, include first four letters of last name.)

Gender (check one) Male Female Unknown

Patient's Date of Birth (mm/dd/yyyy) ___/___/_____

Patient's Zip code (USA) _____

Country of Residence (if not USA) _____

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 data not available
 Unknown: Patient is unsure of race

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: Patient refused or data not available
 Unknown: Patient is unsure of their ethnicity

NCCTG Eligibility Checklist N06CA

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Page 2 of 3

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
Received, or are currently receiving, neurotoxic chemotherapy (including but not limited to taxanes such as paclitaxel or docetaxel; platinum-based compounds such as carboplatin, cisplatin, or oxaliplatin; or vinca alkaloids such as vincristine or vinblastine, or other neurotoxic chemotherapy agents such as bortezomib, lenalidomide or thalidomide). Note: Patients on daily chemotherapy will not be eligible for this trial.	___	___	___
Pain or symptoms of peripheral neuropathy of duration \geq 1 month attributed to chemotherapy.	___	___	___
A score of \geq 4 out of 10 on the numbness/tingling/pain numeric analogue scale (see Appendix VII). Score: _____	___	___	___
\geq 18 years of age. Age = _____.	___	___	___
Ability to sign informed consent and understand the nature of a placebo-controlled trial.	___	___	___
ECOG Performance Status (PS) of 0, 1, or 2. PS = _____.	___	___	___
Ability to complete questionnaires by themselves or with assistance.	___	___	___
Life expectancy \geq 4 months.	___	___	___
Creatinine \leq 1.5 X UNL obtained \leq 90 days prior to registration. Creatinine = _____; UNL = _____ Creatinine Date (mm/dd/yyyy): ____ / ____ / ____	___	___	___
Neuropathy limited to either hands or feet (or both) where gel can be applied.	___	___	___
Women who are not able to bear children. Note: This is defined by those who are menopausal (12 months and no menstrual period if natural menopause), have had a hysterectomy and/or oophorectomy, permanent surgical sterilization (tubal ligation).	___	___	___

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

Contraindications	Yes	No	NA
Pre-existing or history of peripheral neuropathy due to any cause other than chemotherapy (diabetes, alcohol, toxin, hereditary, etc.).	___	___	___
History of an allergic reaction to amitriptyline HCl, baclofen, and/or ketamine.	___	___	___
Treatment \leq 30 days with anticonvulsants, tricyclic antidepressants, MAO inhibitor, or other neuropathic pain medication agents such as carbamazepine, phenytoin, valproic acid, gabapentin, lamotrigine, topical lidocaine patch or gel, capsaicin cream, amifostine, etc. Note: Patients who have taken any of these agents for peripheral neuropathy for \leq 1 week during the past 30 days, but are no longer taking the agent, are not excluded.	___	___	___
Diagnosis of coronary artery disease including but not limited to MI, PTCA, or CABG \leq 5 years or diagnosis of congestive heart failure of any NY heart class I-IV. Note: Valve replacements are permitted as long as patient has fully recovered from the surgery.	___	___	___
Other medical conditions, which in the opinion of the treating physician/allied health professional would make this protocol unreasonably hazardous for the patient.	___	___	___
Current use of any of the study agents in any manner.	___	___	___
Skin abnormalities at the intended application sites (hands and feet) of study gel (i.e.: skin breakdown)	___	___	___
Any of the following: <ul style="list-style-type: none"> • Pregnant • Nursing women • Women of childbearing potential 	___	___	___

All responses in above section must be "No" unless specified as "NA."

NCCTG Eligibility Checklist N06CA

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Patient study ID number _____

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

	Yes	No	NA
Consent form signed and dated. Date of consent ___/___/_____.	___	___	___
Authorization for use and disclosure of protected health information signed and dated. Non-USA institution only (check NA) vs. Date of authorization ___/___/_____.	___	___	___
Treatment on this protocol must commence at the accruing membership under the supervision of an NCCTG member physician or allied health professional.	___	___	___
Treatment cannot begin prior to registration and must begin ≤28 days after registration.	___	___	___
Pretreatment tests/procedures (see Section 4.0) must be completed ≤30 days prior to registration.	___	___	___
Earliest pretreatment test date ___/___/_____; latest pretreatment test date ___/___/_____	___	___	___
All required baseline symptoms (see Section 10.3) must be documented and graded.	___	___	___
Study drug availability is checked.	___	___	___
Patient questionnaire booklet availability checked; copies are not acceptable for this submission.	___	___	___
Translational Research (Mayo Clinic Rochester patients only): An optional translational research component is part of the Continuation Phase of the study for Mayo Clinic Rochester patients only. There will be an option to select if the patient is to be registered onto this component (Section 14.0). • Patient has/has not given permission to give a blood sample for research testing. Not a Mayo Clinic Rochester Patient (check NA).	___	___	___

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

Stratification Factors

Chemotherapy with a neurotoxic agent (select one):

- ___ Active (completed)
___ Non-active (discontinued)

Use of opioids or oral pain medications (select one):

- ___ Yes
___ No

Eligibility Pain Rating (select one – see Section 3.13 and Appendix VII):

- ___ 4 - 7
___ 8 - 10

Previous ineffective pharmacologic treatment for peripheral neuropathy (select one):

- ___ Yes
___ No

Assigned Treatment

___ Amitriptyline HCL/baclofen/ketamine gel vs. placebo

Person registering _____ Signature _____ Reg. office specialist _____ initials

Physician _____ Signature _____ M D Y

NORTH CENTRAL CANCER TREATMENT GROUP
N06CA Continuation Phase Eligibility Checklist

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N06CA: The Use of Topical Baclofen, amitriptyline HCl, and Ketamine (BAK) in a PLO Gel vs. Placebo for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Phase III Randomized Double-Blind Placebo Controlled Study

This study is open to MCR patients only. If the patient and physician want to continue with the active gel, or if on the placebo, begin the active gel, call (507/248-4130) or fax (507/284-0885) a completed continuation phase eligibility checklist to the Registration Office between 8 a.m. and 4:30 p.m. central time Monday through Friday.

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/allied health professional _____
Institution patient number (local subject number) _____
IRB approval date (mm/dd/yyyy) ____/____/____

Patient study ID number _____

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

Registration Check

The double-blind phase of the study must be completed prior to the treatment code being broken; that is, after the treating site has received the completed patient questionnaire booklet.	Yes No ____
--	----------------

All responses in above section must be "Yes"

Assigned Treatment

____ Amitriptyline HCL/baclofen/ketamine gel

Person registering _____ Signature _____ Registration Office Specialist _____ initials

Physician _____ Signature _____ M - D - Y

PLACE LABEL HERE

Protocol Number: N06CA

Patient ID: _____ Patient Initials: _____
L F M

Institution Number: _____

Institution: _____

NORTH CENTRAL CANCER TREATMENT GROUP

**ROCHESTER PATIENTS ONLY
BLOOD SPECIMEN SUBMISSION FORM**

ALL ITEMS MUST BE COMPLETED

Are data amended? (*check one*) Yes No

(if data are amended, please circle in red when using paper form)

Current Cycle Number: _____

INSTRUCTIONS:

*This form is only completed once during weeks 3-4 of double-blind phase. Complete this form for **Rochester patients** and enter into the remote data entry system within 7 days of specimen collection. See Section 14 of the protocol for specimen requirements and shipment.*

Did this patient provide written consent to give blood specimen(s) for research? (*check one*)

1 Yes. If Yes, complete rest of form.

2 No. If No, end form.

Was a research blood specimen collected? (*check one*)

1 Yes. If Yes: Date of collection: (*mm/dd/yyyy*) ___/___/_____

Date Specimen Shipped: (*mm/dd/yyyy*) ___/___/_____

2 No. If No, reason: _____