

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.