

North Central Cancer Treatment Group

N0779: Phase II Study of Vorinostat (SAHA) in Combination with Bortezomib (PS-341) in Patients with Recurrent Glioblastoma Multiforme

Addendum 5 – March 20, 2009

Summary

Administrative/editorial changes.

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

Title page Updated to reflect the addition of Addendum 5 and revised NCI version date.

Schema

Page 4: For clarification purposes, the following has been added to the schema:
Cycle 1 Arm B = up to 30 days in length (**pre-surgery through recovery**)

For clarification purposes, the “Event Monitoring” box has been revised as follows:

Event Monitoring
Every 3 months x 2 years then
every 6 months ~~x 3 years~~ **per**
Section 18.0

Section 4.0

Page 18:

Test Schedule

For clarification purposes, Footnotes #5, 9, and 10 have been revised as follows:

5. Patients undergoing surgery will have a post ~~procedure~~ **surgical** MRI performed **somewhere between** ≤ 7 days after surgery **and but** ≤ 28 days **after surgery** ~~prior to initiation of post surgery treatment.~~
9. All patients (Arms A and B) should submit blocks obtained at time of original diagnosis and recurrence, if applicable. Patients undergoing surgery (Arm B) should also submit tissue obtained at time of the surgery. ~~Note: Tissue samples will also be obtained on the day of surgery.~~ All tissue specimens must be submitted ≤ 30 days following registration.
10. If materials have been previously submitted to Mayo Neuropathology for a consult review, fax a copy of this review to the NCCTG pathology coordinator (507-284-9628) to verify grade 4 astrocytoma. ~~Then follow the pathology material submission timeline found in Section 18.0 so the process can be completed.~~

Appendix IA

Consent Form

Page 3:

Under the “During the study” section, the first sentence of the first paragraph under the bulleted items has been revised for clarification as follows:

You will get vorinostat once daily by mouth **with food (capsules should be taken whole)**, 14 days in a row, and bortezomib into a vein twice weekly (days 1, 4, 8, and 11) during the 14 days that you are also getting vorinostat.

Page 4:

The first row in the table for “Cycle 1” has been revised for clarification as follows:

Days 1 through 14	<ul style="list-style-type: none"> • Begin taking vorinostat once a day by mouth with food (capsules should be taken whole). • Complete the Patient Medication Diary.
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The second row in the table for “Future cycles” has been revised for clarification as follows:

Days 1 through 14	<ul style="list-style-type: none"> • Keep taking vorinostat once a day by mouth with food (capsules should be taken whole). • Complete the Patient Medication Diary.
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Appendix IB

Consent Form

Page 2:

The “Before surgery” section has been revised for clarification as follows:

You will get vorinostat ~~once daily~~ by mouth in the morning **with food (capsules should be taken whole)**, 2 days before the day of surgery, **1 day before the day of surgery**, and on the day of surgery **without food (capsules should be taken whole)**. Bortezomib will be given into a vein ~~on the one day just~~ before surgery following vorinostat. Your surgery will begin within 2 to 3 hours of getting vorinostat and bortezomib. ~~Within 7 days after surgery, you will have an MRI with contrast done for tumor measurement and another MRI with contrast within 21 days of starting treatment.~~ If you have any bad side effects from the vorinostat and/or bortezomib during the 3 days of treatment, the vorinostat and bortezomib will be stopped and you will go to surgery right away.

The fourth sentence in the “After surgery” section has been revised for clarification as follows:

Once you are ready to get treatment again, you will get vorinostat once daily by mouth **with food (capsules should be taken whole)**, 14 days in a row, and bortezomib into a vein twice weekly during the 14 days that you are also getting vorinostat.

Page 3:

The table “Cycle 1” has been completely rewritten to reflect the correct prior to surgery schedule as follows:

Cycle 1

Day	What you do
Days 1 through 14	<ul style="list-style-type: none"> • Begin taking vorinostat once a day by mouth. • Complete the Patient Medication Diary.
Days 1, 4, 8, 11	<ul style="list-style-type: none"> • Bortezomib will be given into a vein right after vorinostat
Weekly	<ul style="list-style-type: none"> • Routine blood tests • If you are on Coumadin, you will have a test to see how your blood is clotting
Days 15-21	<ul style="list-style-type: none"> • No treatment

Day	What you do
Day 22	<ul style="list-style-type: none"> • Return to your doctor’s office for your next exam and to begin the next cycle. • Bring Patient Medication Diary and pill with any remaining pills

Prior to Surgery	What you do
2 days before surgery	<ul style="list-style-type: none"> • Vorinostat once a day by mouth in the morning with food (capsules should be taken whole)
1 day before surgery	<ul style="list-style-type: none"> • Vorinostat once a day by mouth in the morning with food (capsules should be taken whole) • Bortezomib will be given into a vein right after vorinostat
Day of surgery	<ul style="list-style-type: none"> • Vorinostat once a day by mouth in the morning without food (capsules should be taken whole)
Greater then or equal to 7 days after surgery but less then or equal to 28 days after surgery	<ul style="list-style-type: none"> • MRI with contrast

Page 4: The “Days 1 through 14” row in the “Future cycles” section has been revised as follows for clarification:

Future cycles

Day	What you do
Days 1 through 14	<ul style="list-style-type: none"> • Keep taking vorinostat once a day by mouth with food (capsules should be taken whole). • Complete the Patient Medication Diary.

Appendix III

Patient Medication Diary

Page 1: The study medications are only taken once a day. Therefore, it unnecessary to have reference to the a.m. and p.m. and they have been deleted throughout the entire appendix.