

North Central Cancer Treatment Group

N0574: Phase III Randomized Trial of the Role of Whole Brain Radiation Therapy in Addition to Radiosurgery in the Management of Patients with One to Three Cerebral Metastases

Addendum 4 – March 25, 2011

Summary

- Contact Information for the Study Chair has been revised and placed below Dr. Brown's name at the top of the page
- Contact information for Research Base Data Management Specialist has been removed
- Per NCI, the Secondary AML/MDS Report Form will no longer be used. Therefore, Sections 10.0 and 18.0 have been revised accordingly.
- Section 16.22 target accrual has been changed to reflect the observed rate of evaluable patients.
- Section 16.8 table has been adjusted due to changes in target accrual
- Administrative/editorial changes

A replacement protocol is provided. Please replace the current copy with the one attached. Please keep this update with your protocol. Note: for sites participating through NCCTG, replacement pages are provided. Please incorporate into the protocol and keep this update with your protocol.

Title page

Dr. Paul Brown's contact information has been revised with current contact information, as follows:

~~Mayo Clinic~~ **The University of Texas MD Anderson Cancer Center**
~~200 First Street, SW~~ **1515 Holcombe Blvd, Unit 97**
~~Rochester, MN 55905~~ **Houston, TX 77030**
~~507/284-3559~~ **713/563-2415**
507/284-5280 (FAX)
brown.paul@mayo.edu PDBrown@mdanderson.org

Updated to reflect the addition of Addendum 4 and a revised NCI version date.

NCCTG Contact Information

Page 3: Due to the changes with titles of the NCCTG contacts the following information has been modified:

Butch Kvittem
NCCTG Research Base Quality Control Assurance Specialist

Sara M. Braun
NCCTG *Research Base* Research Protocol Specialist-Development
Coordinator

Patricia A. Aggen
NCCTG *Research Base* Research Protocol Specialist-Coordinator

The Research Base Data Management Specialist contact has been removed (Vicki Bryhn). Please contact the NCCTG Research Base Quality Assurance Specialist (QAS) for technical questions regarding electronic form entry.

Section 6.0 Registration/Randomization Procedures (NCCTG members)

Page 17: In Section 6.29 the first web link has been removed, as this link is no longer active. The following text has been removed:

<http://www.usmedicalsupplies.com/productSearch.do?=&grooved&n=20>

Section 10.0 Adverse Event (AE) Reporting and Monitoring

Page 25: Bullet point 2 in Section 10.21 has been revised with current information regarding the AdEERS forms and contact information. Changes are as follows:

In the rare event when Internet connectivity is disrupted, **a 24-hour notification is to be made to NCI by telephone at: 301-897-7497. An electronic report MUST be submitted immediately upon re-establishment of internet connection. Please note that all paper AdEERS forms have been removed from the CTEP website and will NO LONGER be accepted.** a report may be prepared using the Adverse Event Expedited Report—Single Agent or Multiple Agents paper template (accessible from the CTEP Home Page at <http://ctep.cancer.gov>). Contact the NCCTG SAE Coordinator (as identified on the NCCTG Protocol Resources page) for back-up submission instructions.

With the removal of the Secondary AML/MDS Report Form, new Section 10.22 has been added for clarification and the remaining section (now 10.23) has been revised in the second column, as follows:

10.22 Additional Instructions or Exceptions

- **SECONDARY MALIGNANCIES** (defined as “cancer caused by treatment for a previous malignancy”, e.g., treatment with radiation or chemotherapy) are to be reported through AdEERS.
- Secondary malignancies are not considered metastasis of the initial neoplasm. Secondary malignancy is unrelated to the first cancer that was treated, and may occur months or even years after initial treatment.
- **Second Primary malignancy** (malignancy not due to prior treatment) should not be reported through AdEERS.

10.23 Other Required Expedited Reporting

EVENT TYPE	REPORTING PROCEDURE
Secondary AML/MDS	Reporting for this event required during and after completion of study treatment, via AdEERS using CTCAE v3.0: Report Myelodysplasia as “Blood/Bone Marrow - Myelodysplasia” and Leukemias as “Blood/Bone Marrow - Other (Specify, __)” .
Other Grade 4 or 5 Events and/or Any Hospitalizations During Treatment Not Otherwise Warranting an Expedited Report	<p><u>NCCTG Institutions Only:</u> Complete a Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form within 5 working days.</p> <p>If an AdEERS report has been submitted, this form does not need to be submitted.</p> <p>Fax or mail to the NCCTG SAE Coordinator, NCCTG Operations Office, 200 First Street SW, Rochester, MN 55905, Fax (507)284-9628.</p> <p>You must use CTCAE v3.0 for data submission with this form. The events reported on this form must also appear on the Case Report Forms (i.e., routine data) for this study.</p>

Section 16.0 Statistical Considerations

Pages 31/32: Text has been revised in Section 16.22 due to a revision in target accrual. Changes are as follows:

It is our intent to include the 70 patients that have been accrued by Z0300 in our analysis. Based on the given parameters for the power calculation, this protocol requires a total of 112 evaluable patients (i.e. 56 patients in each arm). We **had originally planned** on an over accrual of 35%, i.e. 40 patients, to account for those patients that are not evaluable due to their not completing a neurocognitive evaluation at 3 months (due to death, patient refusal, etc.). **However, the observed rate of patients, after accruing the 152 patients, was 47%, hence, the amount of over accrual has been increased to 112%, i.e. 126 patients.** This results in a total target enrollment sample size of $112 + 40 - 126 = 152 - 238$ patients. **We anticipate pre-registering 310 patients to register a total of 238 patients necessary for the study design and allotted over accrual. In summary, for this protocol, we will accrue an additional $238 - 70$ (those accrued from ACOSOG Z0300) = 168 patients.**

Page 34: In Section 16.8 text has been revised due to a revision in target accrual, as follows:

Ethnic Category	Sex/Gender			
	Females	Males	Unknown	Total
Hispanic or Latino	0	4 2		4 2
Not Hispanic or Latino	72 46	162 104		234 150
Ethnic Category: Total of all subjects*	72 46	166 106		238 152
Racial Category				
American Indian or Alaskan Native	0	3 2		3 2
Asian	0	3 2		3 2
Black or African American	6 4	16 10		22 14
Native Hawaiian or other Pacific Islander	0	2 1		2 1
White	66 39	142 94		208 133
Racial Category: Total of all subjects	72 43	166 109		238 152

Section 18.0 Records and Data Collection Procedures

Page 35: With the removal of the Secondary AML/MDS Report form, the row “Secondary AML/MDS Report Form” has been removed.