

North Central Cancer Treatment Group

N0871, A Phase II Study of Carboplatin (CBDCA), Paclitaxel (TAXOL), and Everolimus (RAD001) in Previously Untreated Patients with Measurable Disease with Cancer of Unknown Primary (CUP)

Addendum 9 – February 10, 2012

Summary

- An updated Investigators Brochure (IB) for Everolimus dated November 7, 2011 has been received. Therefore, the consent form has been updated accordingly.
- Administrative/editorial changes.

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

Title Page Addendum 8 has been added and the NCI version date has been revised.

Protocol Resources

Page 2: Tamra ~~Chomjak~~ is now known as Tamra **Losinski**.

Section 14.0 **Body Fluid Biospecimens**

Page 44: The shipping instructions in Section 14.254 have been updated as follows:
Ship specimens via Priority Overnight service, Monday – Thursday ONLY, to the BAP ~~Shared Resource~~ **Freezer**. Do not send sample on weekends or the day before or day of an observed national holiday.

Appendix I **Consent Form**

Page 9: Due to the receipt of the updated IB for Everolimus, the last bullet under the Rare but serious risk section has been deleted as follows:

- ~~Re-activation of hepatitis infection (if you have previously been diagnosed with hepatitis, which is a type of infection in the liver) (deleted as hepatitis also listed under the Less Likely section)~~

North Central Cancer Treatment Group

A Phase II Study of Carboplatin (CBDCA), Paclitaxel (TAXOL), and Everolimus (RAD001) in Previously Untreated Patients with Measurable Disease with Cancer of Unknown Primary (CUP)

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

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*Investigator having NCI responsibility for this protocol.

Drug Availability

Supplied Investigational Agents: Everolimus (RAD001), Novartis Pharmaceuticals (*IND #105559*) (*NSC #733504*)

Commercial Agents: Carboplatin (CBDCA) and Paclitaxel (TAXOL)

Document History	(Effective Date)	Document History	(Effective Date)
Activation	September 25, 2009	Addendum 5	September 10, 2010
Addendum 1	November 6, 2009	Addendum 6	November 12, 2010
Update 1	November 6, 2009	Update 2	November 12, 2010
Addendum 2	February 5, 2010	Addendum 7	February 18, 2011
Addendum 3	April 16, 2010	Addendum 8	March 25, 2011
Addendum 4	September 10, 2010	Addendum 9	February 10, 2012

Study Participants **Date Activated**

Entire NCCTG September 25, 2009

NCI Version Date: February 1, 2012

Protocol Resource

Add 6

	Questions:	Contact Name:
Patient eligibility*, test schedule, treatment delays/interruptions/adjustments, dose modifications, adverse events, forms completion and submission	Deborah Papenfus NCCTG <i>Research Base</i> Quality Assurance Specialist Phone: (507) 284-4918 Fax: (507) 266-7240 E-mail: papenfus.deborah@mayo.edu	
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Forms completion and submission	Fern G. Lowe NCCTG Member Clinical Research Associate Phone: (306) 655-2669	
Protocol document, consent form, Regulatory issues	Tamra Losinski NCCTG <i>Research Base</i> Research Protocol Specialist Phone: (507) 284-0915 Fax: (507) 284-5280 E-mail: losinski.tamra@mayo.edu	
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Non-paraffin biospecimens	Roxann Neumann, RN, BSN, CCRP NCCTG <i>Research Base</i> Biospecimen Resource Manager Phone: (507) 538-0602 Fax: (507) 266-0824 Email: neumann.roxann@mayo.edu	

* No waivers of eligibility per NCI

Add 3

Add 8,9

14.25 Shipping

14.251 Verify ALL sections of the Blood Specimen Submission Form (see Forms Packet), N0871 Blood Requisition Form (Appendix V), and specimen collection label are completed and filled in correctly. Enter information from the Blood Specimen Submission Form into the remote data entry system ≤ 7 days after specimen collection.

14.252 Specimens must be shipped the same day it is drawn.

14.253 Ship EDTA tube with a properly prepared cold pack. See Appendix IV for specific details for cold pack preparation (i.e., frozen or refrigerated) and proper packing of blood and cold pack to avoid freezing of specimen.

Add 9

14.254 Ship specimens via Priority Overnight service, **Monday – Thursday ONLY**, to the BAP Freezer. **Do not send sample on weekends or the day before or day of an observed national holiday.**

14.255 The submitting institution is responsible for the shipping costs of the specimen for this study.

14.256 BAP will process specimen according to Appendix VI instructions.

14.3 Other Body Fluids Handling (None)

14.4 Study Methodology and Storage Information

14.41 DNA and white blood cells will be extracted from 10 mL EDTA whole blood and stored for future pharmacogenetic assays. Future research may include examining functional polymorphisms in genes that encode protein products involved in the uptake, metabolism, and distribution of carboplatin, paclitaxel, and/or RAD001. Dr. Matthew Ames' laboratory will perform these analyses at a future date. At that time, an aliquot of DNA will be forwarded to Dr. Ames' laboratory and any remaining DNA will be stored frozen by BAP, according to patient consent information (see Section 6.23,) until specific analyses are identified. As protocols are developed, they will be presented for NCCTG and IRB review and approval. (This collection is part of a general strategy of investigation for the majority of NCCTG studies.)

14.5 Return of Genetic Testing Research Results

For this study, DNA specimens are only being banked and no specific genetic testing is being performed. If, at any time, genetic results are obtained that may have clinical relevance, IRB review and approval will be sought regarding the most appropriate manner of disclosure and whether or not validation in a CLIA-certified setting will be required. Sharing of research data with individual patients should only occur when data have been validated by multiple studies and testing has been done in CLIA-approved laboratories.

- Severe cough due to changes in your lung (idiopathic pulmonary infiltrates). A small number of patients that have received RAD001 10 mg daily have reported non-infectious pneumonitis, a condition that affects your lungs. Non-infectious pneumonitis is a known side effect associated with the class of drugs such as RAD001. Non-infectious pneumonitis is frequently of mild intensity and resolves once the study drug is interrupted. A severe form of pneumonitis has been reported in less than 1% of approximately 1000 cancer patients treated to date with RAD001. For this reason, your doctor may ask you to have a chest x-ray or CT at various times during the study to check for this condition. You must contact your doctor immediately if you experience any unusual respiratory or any other symptoms such as a sudden onset of shortness of breath and or coughing and fever as this could be life threatening. You may need to have a chest x-ray or CT or other tests to check your lung function. You may need treatment with corticosteroids or you may need to be admitted to a hospital. In such a case, your doctor will stop the study drug (RAD001 pills) immediately until the cause of these problems have been identified.
- Fluid in the abdomen (ascites) or lungs (pulmonary edema)
- Sad mood (depression)
- Decrease in the ability of the heart to pump blood because of weakening of the heart muscle (congestive heart failure)
- Difficulty urinating

Add 5

Reproductive risks: You should not become pregnant or father a baby while on this study and for 8 weeks following your last dose of study drugs because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control throughout this study and for at least 8 weeks following your last dose of study drug(s). Check with your health care provider about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

For more information about risks and side effects, ask your study doctor.

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 this combination of chemotherapy drugs will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about these medications as a treatment for cancer. 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 cancer.

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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