

North Central Cancer Treatment Group

N057K: Phase I/II Evaluation of Everolimus (RAD001), Radiation and Temozolomide (TMZ) Followed by Adjuvant Temozolomide and Everolimus in Newly Diagnosed Glioblastoma

Addendum 14 – April 1, 2011

Summary

- An updated Investigators Brochure (IB) for Everolimus dated December 14, 2010 has been received. Therefore, the consent forms have been updated accordingly.
- 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 14 and revised NCI version date.

Protocol Resources

Page 2: **Sanna L. McKinzie** has replaced ~~Sara M. Braun~~ as the NCCTG *Research Base* Research Protocol Specialist.

Section 16.0 Statistical Considerations and Methodology

Page 61: The “Males” column for the row “American Indian or Alaskan Native” has been corrected in the minority and gender classification table in Section 16.63 as follows:

American Indian or Alaskan Native	1	01	--	2
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Appendices IA & IB Consent Forms

Pages 4-5: Due to the receipt of the updated IB for Everolimus, the risk sections have been revised as follows:

Likely risks of everolimus (*events occurring greater than 20% of the time*)

- Skin rash
- Inflammation and or sores in the mouth that may make swallowing difficult and are painful (mucositis)
- Feeling tired (fatigue)
- Feeling sick to your stomach (nausea)
- Loss of appetite, not feeling hungry (anorexia)
- Decreased number of blood cells (platelets) that help to clot the blood, which could put you at increased risk of bleeding (thrombocytopenia)
- A low number of white blood cells (infection fighting cells) which could put you at risk for infection (neutropenia)
- Change in taste (dysgeusia)
- Loose stools (diarrhea)
- Headache
- **Infections such as:** (*moved from Less likely*)
 - **cold symptoms, such as runny or stuffy nose (rhinitis)**
 - **sore throat (pharyngitis)**
 - **inflammation/infection of the lungs (pneumonia)**
- **Cough** (*moved from Less likely*)
- **Decrease in red blood cells (oxygen carrying cells), which could make you feel tired**

(**anemia**) (*moved from Less likely*)

- **Elevated levels of cholesterol in the bloodstream, which may lead to heart disease or other health problems (Hyperlipidemia)** (*moved from Less likely*)
- **High blood sugar level (hyperglycemia)** (*moved from Less likely*)
- **Abnormal kidney function (Increased creatinine)** (*newly added*)
- **Loss of strength, weakness (Asthenia)** (*newly added*)

Less likely risks of everolimus (*events occurring less than or equal to 20% of the time*)

- Itching sensation (pruritus)
- Redness of the skin (erythema)
- Pimples on your skin (acne)
- ~~Infections such as:~~ (*moved to Likely*)
 - ~~cold symptoms, such as runny or stuffy nose (rhinitis)~~
 - ~~sore throat (pharyngitis)~~
 - ~~inflammation/infection of the lungs (pneumonia)~~
- Poor wound healing
- High blood pressure (hypertension)
- Low blood pressure (hypotension)
- Swelling in your arms or legs (edema)
- Certain kind of infection of the liver which causes inflammation and can cause liver damage (hepatitis)
- Sensation of lightheadedness or vertigo (spinning sensation) (dizziness)
- Yeast (fungal) infection in the mouth and throat (thrush/oral candidiasis)
- Difficulty passing stool (constipation)
- Swelling of the belly area (abdominal distention)
- Stomach pain (abdominal pain)
- ~~Cough~~ (*moved to Likely*)
- Fever (pyrexia)
- ~~Decrease in red blood cells (oxygen carrying cells), which could make you feel tired (anemia)~~ (*moved to Likely*)
- ~~Elevated levels of cholesterol in the bloodstream, which may lead to heart disease or other health problems (Hyperlipidemia)~~ (*moved to Likely*)
- Throwing up (vomiting)
- Low blood sugar which could be severe (hypoglycemia)
- Impaired glucose tolerance (intermittently raised glucose levels of 140-199 after 2 hours)
- ~~High blood sugar level (hyperglycemia)~~ (*moved to Likely*)
- Decreased sodium levels in the blood (hyponatremia)
- Low potassium levels in the blood (hypokalemia)
- Small red or purple spots on your skin (petechia)
- Fever, aching joints (flu like syndrome)
- Difficulty falling or staying asleep (insomnia)
- Nervousness
- Changes in heart rhythm seen on electrocardiogram
- Inflammation of the foreskin and head of penis (balanitis)
- Inflammation of the urinary bladder (cystitis)
- Profuse bleeding (hemorrhage)