

North Central Cancer Treatment Group

N064B, Randomized Phase II Trial of Panitumumab, Erlotinib, and Gemcitabine vs. Erlotinib and Gemcitabine in Patients with Untreated, Metastatic Pancreatic Adenocarcinoma

Addendum 9 – March 11, 2011

**Summary**

- Contact information for RPS III has been updated
- Contact information for the Data Management Specialist has been removed.
- Based on review of the panitumumab investigator brochure 9.1 dated August 19, 2010 revisions have been made to Section 15.0 and the consent form
- Administrative/editorial changes.

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

**Title page** Revised NCI version date and Addendum 9 have been added.

**Protocol Resources**

Page 2: Contact information has been revised for the Research Protocol Specialist III, as follows:

~~Linda S Long~~ **Sanna McKinzie**  
NCCTG Research Base Research Protocol Specialist III  
Phone: 507-266-3853 **538-6646**  
Fax: 507-284-5280  
E-mail: [long.linda@mayo.edu](mailto:long.linda@mayo.edu) [mckinzie.sanna@mayo.edu](mailto:mckinzie.sanna@mayo.edu)

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

**Section 10.0 Adverse Event (AE) Reporting and Monitoring**

Page 42: The last bullet point in Section 10.21 has been revised with current information, 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 (available on 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.~~

The first row of the table in Section 10.22 has been revised for correction, as follows:

EVENT TYPE	REPORTING PROCEDURE
Secondary AML/MDS	<p>Reporting for this event required during and after completion of study treatment, via AdEERS.</p> <p><del>Through December 31, 2010, continue using CTCAE v3.0: Report Myelodysplasia as “Blood/Bone Marrow – Myelodysplasia” and Leukemias as “Blood/Bone Marrow – Other (Specify, ___)”.</del></p> <p>Beginning January 1, 2011, AdEERS will only accept CTCAE v4.0 for this study: Report these events using “Neoplasms benign, malignant and unspecified (including cysts and polyps)” <i>Other (Specify, ___)</i> <b>and including the appropriate adverse event:</b></p> <ul style="list-style-type: none"> <li>- <b>Leukemia secondary to oncology chemotherapy</b></li> <li><b>OR</b></li> <li>- <b>Myelodysplastic syndrome</b></li> <li><b>OR</b></li> <li>- <b>Treatment related secondary malignancy.</b></li> </ul>

**Section 15.0 Drug Information**

Page 71:

Based on review of the panitumumab investigator brochure 9.1 dated August 19, 2010 revisions have been made to Section 15.344, as follows:

- Allergy/Immunology: Allergic reaction, **in rare circumstances can include the development of antibodies directly against panitumumab, potentially rendering it less effective.**
- Cardiac: Acute myocardial infarction, myocardial infarction, cardio-respiratory arrest, cardiac arrest,
- Constitutional symptoms: Fever, fatigue
- Dermatology/skin: Dermatitis acneiform, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, skin fissures, nail changes, excessive growth of eyelashes, macular-papular rash, **wound dehiscence.** Infectious complications including sepsis, in rare cases leading to death, and abscesses requiring incisions and drainage were reported.
- Gastrointestinal: Stomatitis, mucositis, diarrhea, dehydration, nausea, vomiting, dry mouth, lips, or nose, **intestinal perforation.**
- Hemorrhage/bleeding: Nose bleeds...

**Appendix I** **Consent Form**

Pages 11/12:

Based on review of the panitumumab investigator brochure 9.1 dated August 19, 2010 revisions have been made to the “Rare but serious risks of panitumumab” and a paragraph located after this section. Changes are as follows:

Rare but serious risks of panitumumab (*events occurring less than 2-3% of the time*)

- Collection of fluid in the space around the lung (pleural effusion)
- Fever, chills, swelling of body, shortness of breath (allergic reaction)
- Inflammation/infection of the lungs (pneumonitis)
- Scarring of the lungs (pulmonary fibrosis)
- Swelling in the body, especially in the arms and legs (edema)
- Blood clots in the lungs which could be life threatening or cause death (pulmonary embolism)
- Blood clot in vein (deep vein thrombosis)
- Inflammation of veins (phlebitis)
- High blood pressure (hypertension)
- Lack of oxygen to the heart muscle which can cause damage to the heart (heart attack)
- Heart stops beating, which can cause death (cardiac arrest)
- Breathing stops, which can cause death (respiratory arrest)
- Lack of oxygen to the brain caused by either bleeding in the brain or blood clot. Also called a stroke (cerebrovascular accident)
- **Infection that has spread to the bloodstream and can cause low blood pressure, fever, and/or death (sepsis)**
- **Development of a hole or tear in the intestine, which can cause damaging intestinal fluids to leak into the abdominal cavity, resulting in bleeding, severe pain, fever, nausea, vomiting, infection and possibly death (intestinal perforation)**
- **Breakdown of a wound that has already healed (wound dehiscence)**

The risks of panitumumab used in pancreatic cancer with other agents is unknown.

As with any medication, allergic reactions are a possibility. **In rare circumstances the reaction can include the development of antibodies (special kinds of proteins produced by the immune system designed to recognize and stop foreign substances in the body) directly against panitumumab, potentially rendering it less effective.**

## North Central Cancer Treatment Group

**Randomized Phase II Trial of Panitumumab, Erlotinib, and Gemcitabine vs. Erlotinib and Gemcitabine in Patients with Untreated, Metastatic Pancreatic Adenocarcinoma**

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

Study Chairs: George P. Kim, M.D. (Research Base)\*  
Mayo Clinic  
4500 San Pablo Road  
Jacksonville, FL 32224  
904/953-2000  
507/284-5280 (FAX)  
[kim.george@mayo.edu](mailto:kim.george@mayo.edu)

Muhammas Salim, M.D. (NCCTG)

Study Co-chairs: Thomas C. Smyrk, M.D. (Pathology – Research Base) ✓  
Ann E. McCullough, M.D. (Pathology – NCCTG)  
Monica M. Reinholz, Ph.D. (Laboratory – Research Base) ✓  
Daniel D. Billadeau, Ph.D. (Laboratory – Research Base) ✓  
Robert B. Jenkins, M.D. (Laboratory – Research Base) ✓  
Matthew M. Ames, Ph.D. (Laboratory – Research Base) ✓  
Stephen N. Thibodeau, Ph.D. (Laboratory – Research Base) ✓

Statistician: Nathan R. Foster, M.S. ✓  
507/284-8803

**Drug Availability**

**DCTD Supplied Investigational Agents:** None

**Commercial Agents:** Gemcitabine

**Drug Company Supplied:** Erlotinib (Genentech), Panitumumab (Amgen) – IND # 102462

**\*Investigator having NCI responsibility for this protocol**

✓Study contributor(s) not responsible for patient care.

<b>Document History</b>	<b>(Effective Date)</b>	<b>Document History</b>	<b>(Effective Date)</b>
Activation	March 27, 2009	Addendum 5	April 2, 2010
Addendum 1	May 15, 2009	Addendum 6	June 11, 2010
Addendum 2	June 5, 2009	Addendum 7	July 23, 2010
Addendum 3	July 24, 2009	Addendum 8	October 15, 2010
Addendum 4	November 27, 2009	Addendum 9	March 11, 2011

**Study Participants      Date Activated**

Entire NCCTG      March 27, 2009

NCI Version Date: March 2, 2011

Add 9

## Protocol Resources

Questions:	Contact Name:
Patient eligibility*, test schedule, treatment delays/interruptions/adjustments, dose modifications, adverse events, forms completion	<b>Deb J. Papenfus</b> NCCTG <i>Research Base</i> Quality Assurance Specialist Phone: 507/284-4918 Fax: 507/266-7240 E-mail: <a href="mailto:papenfus@mayo.edu">papenfus@mayo.edu</a>
Drug administration, infusion pumps, nursing guidelines	<b>Jerri K. Spohn, R.N.</b> NCCTG <i>Research Base</i> Nurse Phone: 507/284-2459 E-mail: <a href="mailto:lee.jeraldine@mayo.edu">lee.jeraldine@mayo.edu</a> <b>Colleen Sweetland, R.N.</b> NCCTG Member Nurse Phone: 734/712-5796 E-mail: <a href="mailto:sweetlac@trinity-health.org">sweetlac@trinity-health.org</a>
Forms completion and submission	<b>Beth Bement-Stump</b> NCCTG Member Clinical Research Associate Phone: 605/719-6075 Fax: 605/719-2310 E-mail: <a href="mailto:ebement@rcrh.org">ebement@rcrh.org</a>
Protocol document, consent form, Regulatory issues	<b>Sanna McKinzie</b> NCCTG <i>Research Base</i> Research Protocol Specialist III Phone: 507/538-6646 Fax: 507/284-5280 E-mail: <a href="mailto:mckinzie.sanna@mayo.edu">mckinzie.sanna@mayo.edu</a>  <b>Patricia A. Aggen</b> NCCTG <i>Research Base</i> Research Protocol Specialist II Phone: 507/538-6232 Fax: 507/284-5280 E-mail: <a href="mailto:aggen.patricia@mayo.edu">aggen.patricia@mayo.edu</a>
Adverse Events	<b>Patricia G. McNamara</b> NCCTG <i>Research Base</i> AdEERS Coordinator Phone: 507/266-3028 Fax: 507/284-9628 E-mail: <a href="mailto:mcnamara.patricia@mayo.edu">mcnamara.patricia@mayo.edu</a>
Paraffin-embedded Tissue Pathology	<b>Jennifer S. Mentlick</b> NCCTG <i>Research Base</i> Pathology Coordinator Phone: 507/293-3928 Fax: 507/284-9628 E-mail: <a href="mailto:mentlick.jennifer@mayo.edu">mentlick.jennifer@mayo.edu</a>
Non-paraffin Biospecimens	<b>Roxann Neumann, R.N., B.S.N., C.C.R.P.</b> NCCTG <i>Research Base</i> Biospecimen Resource Manager Phone: 507/538-0602 Fax: 507/266-0824 E-mail: <a href="mailto:neumann.roxann@mayo.edu">neumann.roxann@mayo.edu</a>

\* No waivers of eligibility per NCI

**Additional Instructions or Exceptions to AdEERS Expedited Reporting Requirements**

**Within 1 working day of notification of an SAE**, the NCCTG SAE Coordinator will notify:

- The NCCTG IND Coordinator who will notify the FDA as warranted by the event and stipulated in the U.S. Code of Federal Regulations.
- Genentech BioOncology Drug Safety Department (FAX: 650/225-4682 or 650/225-5288).
- Amgen Global Safety (FAX: 888/814-8653).
- 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

Add 9

10.22 Other Required Expedited Reporting

<u>EVENT TYPE</u>	<u>REPORTING PROCEDURE</u>
<p>Secondary AML/MDS</p>	<p>Reporting for this event required during and after completion of study treatment, via AdEERS.</p> <p><b>Beginning January 1, 2011, AdEERS will only accept CTCAE v4.0 for this study:</b> Report these events using “Neoplasms benign, malignant and unspecified (including cysts and polyps)” <i>and including the appropriate adverse event:</i></p> <ul style="list-style-type: none"> <li>- Leukemia secondary to oncology chemotherapy</li> <li>OR</li> <li>- Myelodysplastic syndrome OR</li> <li>- Treatment related secondary malignancy.</li> </ul>
<p>Other Grade 4 or 5 Events and/or Any Hospitalizations During Treatment Not Otherwise Warranting an Expedited Report</p>	<p>If an AdEERS report has been submitted, this form does not need to be submitted.</p> <p>Submit the NCCTG Notification Form Grade 4 or 5 Non-AER Reportable Events/Hospitalization electronically via the NCCTG Remote Data Entry System within 5 working days of the date the CRA is aware of the event(s) necessitating the form, using CTCAE v3.0.</p> <p>The NCCTG SAE Coordinator will notify the NCCTG IND Coordinator who will submit to the FDA IND as warranted by the event and stipulated in the U.S. Code of Federal Regulations.</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>

Add 8,9

Add 1,4,9

## 15.344 Known and anticipated risks

- Allergy/Immunology: Allergic reaction, in rare circumstances can include the development of antibodies directly against panitumumab, potentially rendering it less effective.
- Cardiac: Acute myocardial infarction, myocardial infarction, cardio-respiratory arrest, cardiac arrest,
- Constitutional symptoms: Fever, fatigue
- Dermatology/skin: Dermatitis acneiform, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, skin fissures, nail changes, excessive growth of eyelashes, macular-papular rash, wound dehiscence. Infectious complications including sepsis, in rare cases leading to death, and abscesses requiring incisions and drainage were reported.
- Gastrointestinal: Stomatitis, mucositis, diarrhea, dehydration, nausea, vomiting, dry mouth, lips, or nose, intestinal perforation
- Hemorrhage/bleeding: Nose bleeds
- Infection: Infection, sepsis, abscess
- Laboratory/metabolic: Hypomagnesemia, hypocalcemia, hypokalemia
- Ocular/visual: Eye changes including dryness, itching, increased tearing and redness
- Pain: Headache
- Pulmonary/Upper Respiratory: Dyspnea, cough, dyspnea exertional, interstitial lung disease, pleural effusion, pneumonitis, respiratory arrest, pulmonary fibrosis
- Vascular: Peripheral edema, edema, pulmonary embolism, hypertension, and cerebrovascular accident, deep vein thrombosis, and superficial thrombophlebitis

15.35 Drug procurement: Panitumumab will be supplied by Amgen, Inc. Each institution will order the drug from the NCCTG research base pharmacist using the Clinical Drug Request Form available at <https://ncctg.mayo.edu/ncctg/forms/NonProtocolSpecificForms/ClinicalDrugRequestForm.pdf>. Submit the NCCTG Clinical Drug Request Form to:

Medical Oncology Pharmacist  
Mayo Clinic  
Gonda 10-178  
Rochester, MN 55905  
FAX (507) 284-3464

Outdated or unused drug should be destroyed on-site in accordance with the SOPs in place at each participating NCCTG site.

**Panitumumab:**

Add 1

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

- Rash that looks like acne or pimples (macular-papular rash)
- Dry skin (xerosis)
- Itching sensation (pruritis)
- Cracks in the skin from excessive dryness (fissures)
- Redness of the skin (erythema)
- Peeling of the skin (skin exfoliation)
- An infection where the nail and skin meet at the side or the base of a finger or toenail, which can be painful (paronychia)
- Tiredness (fatigue)
- Loose stools (diarrhea)

Add 1,5

**Less likely risks of panitumumab** (*events occurring less than 20% of the time*)

- Low levels of magnesium in the blood (hypomagnesemia)
- Low potassium levels in the blood (hypokalemia)
- Abnormally low calcium in your blood stream that can result in muscle cramps, abdominal cramps, or spasms (hypocalcemia)
- Inflammation and/or sores in the mouth that may make swallowing difficult and are painful (mucositis)
- Shortness of breath or difficulty breathing (dyspnea)
- Cough
- Excessive or abnormal loss body fluid (dehydration)
- Feeling sick to your stomach (nausea)
- Throwing up (vomiting)
- Headaches
- Nail changes
- Excess growth of eyelashes
- Eye changes including dryness, itching, increased tearing, redness, possible infection
- Dryness in mouth, lips or nose
- Nose bleeds (Epistaxis)
- Fever (Pyrexia)
- Skin infection

Add 1,5,9

**Rare but serious risks of panitumumab** (*events occurring less than 2-3% of the time*)

- Collection of fluid in the space around the lung (pleural effusion)
- Fever, chills, swelling of body, shortness of breath (allergic reaction)
- Inflammation/infection of the lungs (pneumonitis)
- Scarring of the lungs (pulmonary fibrosis)
- Swelling in the body, especially in the arms and legs (edema)
- Blood clots in the lungs which could be life threatening or cause death (pulmonary embolism)
- Blood clot in vein (deep vein thrombosis)
- Inflammation of veins (phlebitis)
- High blood pressure (hypertension)
- Lack of oxygen to the heart muscle which can cause damage to the heart (heart attack)
- Heart stops beating, which can cause death (cardiac arrest)
- Breathing stops, which can cause death (respiratory arrest)
- Lack of oxygen to the brain caused by either bleeding in the brain or blood clot. Also called a stroke (cerebrovascular accident)
- Infection that has spread to the bloodstream and can cause low blood pressure, fever, and/or death (sepsis)
- Development of a hole or tear in the intestine, which can cause damaging intestinal fluids to leak into the abdominal cavity, resulting in bleeding, severe pain, fever, nausea, vomiting, infection and possibly death (intestinal perforation)
- Breakdown of a wound that has already healed (wound dehiscence)

The risks of panitumumab used in pancreatic cancer with other agents is unknown.

Add 9 As with any medication, allergic reactions are a possibility. In rare circumstances the reaction can include the development of antibodies (special kinds of proteins produced by the immune system designed to recognize and stop foreign substances in the body) directly against panitumumab, potentially rendering it less effective.

The risks of drawing blood include pain, bruising or rarely infection at the needle site.

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study **or for 2 months after stopping panitumumab**. It is important you understand that you need to use birth control while on this study **and for 6 months after stopping panitumumab**. 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. Some of the drugs used in the study may make you unable to have children in the future.

You will be required to have a pregnancy test before starting on the study if you are a woman of childbearing age.

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 that combining gemcitabine, erlotinib, and panitumumab 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 gemcitabine, erlotinib, and panitumumab as treatments 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.