

North Central Cancer Treatment Group

N064A, Phase II Study of Panitumumab, Chemotherapy, and External Beam Radiation in Patients with
Locally Advanced Pancreatic Cancer

Addendum 4 – July 9, 2010

Summary

- Updated drug information for gemcitabine has been received.
- Consent form has been revised to include updated risk information for gemcitabine
- Administrative/Editorial changes.

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

Title Page The Addendum 4 has been added and the NCI version date has been updated.

Section 4.0 **Test Schedule**

Page 21: Footnote 12 has been revised to clarify the timepoints for blood collection and to specify that blood collection is to occur during panitumumab therapy.

Kits are required. Blood is to be collected after registration but prior to first treatment, Cycle 1 day 8 (7 days [±24 hours] after first panitumumab dose), prior to treatment cycle 3 day 1 (4-6 weeks after RT at start of gemcitabine treatment), prior to treatment cycle 4 day 15 and cycle 6 day 1, **prior to cycle 7 day 15, prior to cycle 9 day 1, and prior to cycle 11 day 15 (i.e., every 6 weeks until completion of gemcitabine and/or panitumumab treatment [post-chemo/RT] and panitumumab maintenance therapy)**, and at recurrence....

Section 14.0 **Body Fluid Biospecimens**

Pages 55 & 57: The biospecimen shipping instructions have been updated as follows:

14.212 ...Do not send unused kits back to ~~MML~~ **BAP**.

14,213 ...Kits will arrive inside the ~~berry-colored~~ shipping boxes.

14.251 ...~~MML~~ **Biospecimen Accessioning and Processing (BAP)** Requisition Form (provided in kit), and specimen collection labels are completed and filled in correctly.

14.254 ...Ship specimens via Priority Overnight service, **Monday – Thursday ONLY**, to ~~Mayo Medical Laboratories (MML)~~ **BAP** according to kit instructions.

14.255 The ~~MML BAP~~ kits will contain a smart shipper label (white barcoded label) affixed to the ~~berry-colored~~ shipping boxes. The smart shipper label is a pre-addressed return label, which replaces the need for an airbill. Shipping costs will be covered by NCCTG if this berry colored box is used for shipping specimens to ~~MML BAP~~.

14.256 ~~MML BAP Receiving~~ will ~~receive the samples and immediately~~ forward specimens to the NCCTG Research Base Biospecimens Accessioning and Processing (BAP) Shared Resource, Stabile 13-10A, Attention: BAP Supervisor.

Page 56: In the table in Section 14.241, column 8 has been modified to clarify that blood collection is to occur during panitumumab therapy.

Prior to treatment cycle 4 day 15 and cycle 6 day 1 (every 6 wks until completion of gemcitabine and/or panitumumab treatment **and panitumumab maintenance therapy**)

Section 15.0 Drug Information

Pages 69-72: Due to an updated drug information template for gemcitabine, Section, 15.3 has been replaced in its entirety. The Nursing guidelines in this section have been renumbered accordingly.

Appendix I Consent Form

Page 6: In the Section “During Step 3 (panitumumab only),” a correction has been made to move the blood tests checking for hemoglobin, white blood cells and platelets from “Weekly” to “every other week.” The item has been combined with the one already there.

Weekly

- ~~Blood tests every other week to check for your hemoglobin, white blood cells and platelets.~~

Every other week

- Routine blood tests to check **your hemoglobin, white blood cells and platelets and to see** how well your liver, kidneys, and other....

Pages 13-15: The risks and side effects of gemcitabine have been updated based on the new template for Section 15.3.

Likely risks of gemcitabine (*events occurring greater than 20% 10% of the time*)

- Decrease in white blood cells (may increase chance of developing an infection).
- Decrease in red blood cells (may cause feelings of being tired).
- Decrease in platelets (may increase the chance of bruising or bleeding after injury).
- Nausea (feeling sick to your stomach).
- Vomiting (being sick).
- **Inflammation of the mucous membranes of the mouth and throat (stomatitis).** (*Moved from Less Likely*)

- Flu-like symptoms, including fever, headaches, mild chills, muscle soreness, fatigue, weakness, lethargy, loss of appetite, cough, runny nose, and sweating.
- Changes in liver function tests (tests that show how your liver is working). These changes are usually mild and non-progressive and rarely require stopping treatment with gemcitabine.
- Diarrhea.
- **Constipation.** *(new)*
- Temporary red itchy rash.
- **Itchiness (pruritus).** *(new)*
- Shortness of breath.
- ~~Tingling, prickling, or creeping feeling on the skin~~ *(moved to Less Likely)*
- Fluid retention (usually seen as swelling of the hands, feet, or face) (**peripheral edema**).
- **Pain.** *(new)*
- **Fever.** *(new)*
- **Drowsiness, sleepiness (somnia)** *(moved from Less likely and reworded)*
- **Hair loss (alopecia).** *(moved from Less likely)*
- **Infection.** *(new)*
- **Bleeding (hemorrhage).** *(new)*
- **Blood or protein in the urine (hematuria or proteinuria) or changes in kidney function tests (blood urea nitrogen or BUN levels).** *(moved from Less likely and reworded)*

Less likely risks of gemcitabine *(events occurring less than or equal to 20%-10% of the time)*

- ~~Loss of appetite~~ *(Moved to Rare but serious)*
- Agitation (feeling restless).
- ~~Sleepiness.~~ *(Moved to Likely)*
- ~~Inability to sleep~~ *(moved to Rare but serious)*
- ~~Mild effect on the kidneys (blood or protein in the urine)~~ *(moved to Likely and reworded)*
- ~~Mild hair loss~~ *(moved to Likely and reworded)*
- ~~Inflammation of the mucous membranes of the mouth and throat~~ *(moved to Likely and reworded)*
- **Changes in kidney function test (creatinine levels).** *(reworded)*
- **Injection site reactions.** *(new)*
- **Sudden tightening of the muscles in the small airways in the lung (bronchospasm).** *(new)*
- **Tingling, prickling, or creeping feeling on the skin (paresthesia).** *(moved from Likely)*

Rare but serious risks of gemcitabine (*events occurring less than 2–3% 1% of the time*)

- Fast or irregular heart beat (**arrhythmia**).
- Decreased blood pressure.
- Severe changes in liver function tests (~~including changes that may cause jaundice~~).
- **Severe toxicity to the liver or liver failure.** (*new*)
- Severe difficulty breathing, **including respiratory failure.**
- **Adult Respiratory Distress Syndrome (ARDS) which is sudden failure of the respiratory system due to fluid build-up in the air sacs in the lungs.** (*new*)
- **Excess fluid in the lungs (pulmonary edema).** (*new*).
- **Inflammation of the lung that causes scarring of the lungs and difficulty breathing (interstitial lung disease).** (*new*)
- **Scarring of the lungs that stiffens the lungs and makes breathing difficult (pulmonary fibrosis).** (*new*)
- Severe effects on the kidneys, ~~sometimes leading to kidney failure~~ **including hemolytic uremic syndrome (HUS), a condition which may lead to kidney failure.** (*new*).
- Heart failure.
- **Heart attack (myocardial infarction).** (*new*).
- Confusion.
- Convulsions.
- Coma.
- Severe allergic reactions (**anaphylactoid reaction**). Symptoms may include rash, changes in blood pressure, swelling and increased fluid in the tissues, increases in heart rate, difficulty breathing and collapse.
- Blood vessel inflammation **in the arms and legs (peripheral vasculitis)** and gangrene (death of soft tissue due to lack of blood supply).
- **Whole-body inflammation caused by bacteria in the bloodstream (sepsis).** (*new*).
- Capillary leak syndrome, which can cause low blood pressure or reduced the amount of oxygen getting to tissue.
- Severe skin reactions, including peeling of the skin **and skin infection (cellulitis).** (*new*)
- Blistering red sores in the mucous membranes or larger areas of the body).
- **Small red or purple spots on the body caused by bleeding into the skin (petechiae).** (*new*)
- **Rash or skin reactions in areas that have previously been treated with radiation (radiation recall).** (*new*)
- **Loss of appetite (anorexia).** (*moved from Less Likely*)
- **Chills.** (*new*)
- **Cough.** (*new*)
- **Runny or stuffy nose (rhinitis).** (*new*)
- **Extreme sweating or perspiration (diaphoresis).** (*new*)
- **Headache.** (*new*)

- **Weakness.** (*new*)
- **High blood pressure (hypertension)** (*new*)
- **Sleeplessness (insomnia).** (*moved from Less Likely*)
- **A general feeling of fatigue and discomfort (malaise).** (*new*)
- **Stroke** (*new*)