

North Central Cancer Treatment Group

N083E, Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in Early Breast Cancer

Addendum 3 – May 14, 2010

Summary

- An updated Comprehensive Adverse Events and Potential Risks list (CAEPR) for Lapatinib (version 2.4, dated January 6, 2010) and Trastuzumab (version 2.1, dated March 23, 2010) have been received from the National Cancer Institute (NCI). Therefore, the Drug Information sections and consent form 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 Addendum 3 and the NCI version date.

Section 14.0 **Body Fluid Biospecimens**

Page 44: The biospecimen shipping information has been updated as follows:

- 14.251 Verify ALL sections of the Blood Specimen Submission Form (see Forms Packet), **MCTS Biospecimen Accessioning and Processing (BAP)** Requisition Form (provided in kit), and specimen collection labels 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 (see Forms Packet).
- 14.254 Ship specimens via Priority Overnight service, **Monday – Thursday ONLY**, to ~~Mayo Medical Laboratories (MML)~~ **BAP**. Do not send samples on weekends or holidays.
- 14.255 White, bar coded addressed Ship Manager mailing labels will be affixed to the shipping boxes for shipping specimens to ~~MML~~ **BAP**.
- 14.256 ~~MML~~ **BAP Receiving** will receive the samples and forward specimens immediately to the NCCTG Research Base Biospecimens Accessioning and Processing (BAP) Shared Resource, Stable 13-10A, Attention: BAP Supervisor.

Section 15.0 **Drug Information**

Pages 52-55: Due to the receipt of the updated CAEPR for Trastuzumab, Section 15.36 has been replaced in its entirety.

Pages 57-59: Due to the receipt of the updated CAEPR for Lapatinib, Section 15.47 has been replaced in its entirety.

Pages 52-77: Due to the inclusion of the updated CAEPRs for Trastuzumab and Lapatinib, repagination has occurred.

Appendix I

Page 1:

Consent Form

Version date is revised.

Pages 8-9:

Due to the receipt of the updated CAEPR for Trastuzumab, the risks section for lapatinib updated as follows:

Likely (more than 20% of people taking Trastuzumab have these effects)

- ~~Body pain (muscles, joints, abdomen)~~ *(moved to Less likely and wording expanded)*
- ~~Headache~~ *(moved to Less likely and wording expanded)*
- ~~Weakness, fatigue (feeling very tired, run down)~~ *(deleted)*
- ~~Fever~~ *(moved to Less likely)*
- ~~Chills~~ *(moved to Less likely)*
- ~~Nausea (feeling sick to your stomach)~~ *(moved to Less likely)*
- ~~Vomiting (throwing up)~~ *(moved to Less likely)*
- ~~Diarrhea (loose stools)~~ *(moved to Less likely)*
- ~~Shortness of breath~~ *(moved to Less likely)*
- ~~Cough~~ *(moved to Less likely)*

Less likely (20% or less of people taking trastuzumab have these effects)

- **Skin Rash with the presence of macules (flat discolored area) and papules (raised bump)** *(wording expanded)*
- Hives, itching
- Infection (pneumonia, urinary tract, etc.)
- Loss of appetite (not feeling hungry, not wanting to eat)
- ~~Low white blood cell count, which may increase the risk of infection, and/or slower healing~~ *(separated into individual entries below)*
- **Decreased number of a type of white blood cell (neutrophil/granulocyte)** *(separated from entry above)*
- **Decrease in the total number of white blood cells (leukocytes)** *(separated from entry above)*
- Low red blood cell count, which may result in anemia, tiredness, and/or shortness of breath
- ~~Liver problems (as seen on a blood test)~~ *(separated into individual entries below)*
- **Increased blood level of a liver or bone enzyme (alkaline phosphatase)** *(separated from Liver problems entry above)*
- **Increased blood level of a liver enzyme (AST/SGOT)** *(separated from Liver problems entry above)*
- **Increase blood level of a liver enzyme (GGT)** *(separated from Liver problems entry above)*
- ~~Trouble sleeping (insomnia)~~ *(deleted)*
- ~~Dizziness~~ *(deleted)*
- ~~Depression (feeling down or blue)~~ *(deleted)*
- **Stuffy or Runny nose, sneezing** *(wording expanded)*
- ~~Sore throat~~ *(deleted)*
- Sores in the mouth and throat
- ~~Voice changes (hoarseness)~~ *(deleted)*
- **Body pain (muscles, joints, abdomen, back, bone)** *(moved from Likely and wording expanded)*
- **Headache or head pain** *(moved from Likely and wording expanded)*
- **Fever** *(moved from Likely)*
- **Chills** *(moved from Likely)*
- **Nausea (feeling sick to your stomach)** *(moved from Likely)*
- **Vomiting (throwing up)** *(moved from Likely)*
- **Diarrhea (loose stools)** *(moved from Likely)*
- **Shortness of breath** *(moved from Likely)*
- **Cough** *(moved from Likely)*

- **High blood pressure** (*moved from Rare but serious*)
- **Fast heartbeat; regular rhythm** (*moved from Rare but serious and separated into individual entry from Damage to the heart*)
- **Fast heartbeat usually originating in an area located above the ventricles** (*moved from Rare but serious and separated into individual entry from Damage to the heart*)
- **Fever associated with dangerously low levels of a type of white blood cell (neutrophils)** (*newly added*)
- **The heart stops pumping blood** (*newly added*)
- **A condition in which the heart muscle is abnormally enlarged or thickened** (*newly added*)
- **Decrease in the heart's ability to pump blood during the "active" phase of the heart beat (systole)** (*newly added*)
- **Fluid in the sac around the heart** (*newly added*)
- **Fatigue or tiredness** (*newly added*)
- **Flu-type symptoms (including body aches, fever, chills, tiredness, loss of appetite, cough)** (*newly added*)
- **Chest pain not heart-related** (*newly added*)
- **Pain** (*newly added*)
- **Reaction during the infusion of a drug which may be life-threatening and may result in low blood pressure, fever, chills, difficulty breathing and kidney damage** (*newly added*)
- **Increased blood level of a heart muscle protein (troponin I) indicating damage to the heart muscle** (*newly added*)
- **Pain in the area of the tumor** (*newly added*)
- **Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning** (*newly added*)
- **Severe potentially life-threatening damage to the lungs which can lead to fluid in the lungs** (*newly added*)
- **Sudden constriction of the muscles in the walls of the bronchioles (small airways of the lung)** (*newly added*)
- **Decrease in the oxygen supply to a tissue** (*newly added*)
- **Build up of a large amount of fluid between the layers of tissue that line the lungs and chest cavity** (*newly added*)
- **Inflammation (swelling and redness) of the lungs** (*newly added*)
- **Acne** (*newly added*)
- **Low blood pressure** (*newly added*)
- **Inflammation (swelling and redness) of the sac around the heart** (*newly added*)

Rare but serious risks of trastuzumab which may or may not be related to the drug, but which have been seen in fewer than 2-3% of patients receiving trastuzumab

- ~~Allergic reaction (including life-threatening low blood pressure, shortness of breath and death)~~ (*separated into individual entries below*)
- **Abnormal reaction of the body to substances, called allergens, that are contacted through the skin, inhaled into the lungs, swallowed, or injected (allergic reaction)** (*separated from Allergic reaction above*)
- **Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness** (*separated from Allergic reaction above*)
- ~~Damage to the heart (including abnormal rhythms, damage to the heart muscle)~~ (*moved to Less likely and separated into individual entries*)
- ~~High blood pressure~~ (*moved to Less likely*)
- ~~Neuropathy (numbness, tingling, or other nerve problems, usually in hands and feet)~~ (*deleted*)
- ~~Interstitial pneumonitis – inflammation (swelling) in the lungs (may have trouble breathing)~~
- **Abnormal build up of fluid in the lungs** (*newly added*)

The following section has been deleted:

~~The following side effects have been reported for patients taking part in other trastuzumab research studies. It is not known if these side effects were related to trastuzumab:~~

- ~~• Low platelets which may increase risk of bleeding~~
- ~~• Leukemia or pre-leukemia~~
- ~~• Pancreatitis (swelling of the pancreas)~~
- ~~• Colitis (damage to colon that causes severe diarrhea)~~
- ~~• Kidney problems including kidney failure~~
- ~~• Deafness~~
- ~~• Neurological problems (meningitis, swelling of the brain, thinking abnormalities)~~
- ~~• Liver problems including liver damage or liver failure (jaundice and/or hepatitis)~~
- ~~• Serious breathing problems~~
- ~~• Fluid retention (swelling of ankles or feet, or fluid in the lungs)~~

Pages 9-10:

Due to the receipt of an updated CAEPR for Lapatinib, the risks section has been revised as follows:

Lapatinib possible side effects:

Likely risks of lapatinib (happen >20% of the time)

- Nausea (feeling sick to stomach)
- Loose stools (diarrhea)
- Rash/flaking or shedding of outer layer of skin

Less likely risks of lapatinib (happen ≤20% of the time)

- Acne; pimples
- Itching
- Headache **or head pain** (*wording expanded*)
- Flatulence (passing gas)
- Heartburn or sour stomach
- Abdominal (belly) pain
- Vomiting (throwing up)
- Dehydration (loss of fluid in the body)
- Loss of appetite (not feeling hungry, not wanting to eat)
- Flu-like symptoms (achy, stuffy head, fever, **chills, tiredness, loss of appetite, cough**) (*wording expanded*)
- Sudden reddening of the face and/or neck
- Sores in the mouth and throat and irritation or sores in the lining somewhere in the gastrointestinal tract
- Taste changes
- Liver problems as seen on a blood test (ALT/SGPT, AST/SGOT)
- Elevation of a liver pigment (bilirubin) in the blood that may be a sign of liver problems
- Fatigue (feeling very tired, run down, or weak)
- ~~Nail changes~~ **Loss of some or all of the finger or toenails** (*reworded*)
- Feeling of fullness and tightness in the belly

Rare but serious risks of lapatinib (seen in fewer than 2-3% of patients receiving lapatinib)

- Abnormal electrical conduction within the heart (prolonged QTc interval)
- Decrease in heart's ability to pump blood during the "active" phase of the heartbeat (systole)

- Liver problems/liver failure. Liver damage may cause itching, yellow eyes or skin, dark urine, pain or discomfort in the right upper area of the belly. Tell your doctor immediately if you get any of these symptoms. Your doctor will order simple blood tests to check how your liver is working.
- Inflammation (**swelling and redness**) of the lungs (*wording expanded*)
- Allergic reaction (may include fever, chills and skin rash. Less commonly, the symptoms may include weezing, difficulty breathing, drop in blood pressure, or swelling of the throat.