

North Central Cancer Treatment Group

N0626: A Phase II Randomized Study of Pemetrexed With Sorafenib versus Pemetrexed Alone as Second-line Therapy in Patients With Advanced Non-Small Cell Lung Cancer

Addendum 10 – May 21, 2010

Summary

- An updated Comprehensive Adverse Events and Potential Risks (CAEPR) for Sorafenib (version 2.3, dated February 18, 2010) has been received from the National Cancer Institute (NCI). Therefore, the Drug Information section and consent form have been updated accordingly.
- Administrative changes.

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

Title page Updated to reflect Addendum 10 and revised NCI version date.

Protocol Resources

Page 2: **Rachael Meyers** replaces ~~Sarah Hanson~~ as the NCCTG *Research Base* Quality Assurance Specialist.

Kristine M. Hacker, R.N. replaces ~~Dianne M. Herrera, R.N.~~ as the NCCTG *Research Base* Nurse.

Section 14.0

Pages 39-41:

Body Fluid Biospecimens

Kit instructions have been updated as follows:

- 14.212 Participating institutions may obtain kits by completing and faxing the N0626 **Biospecimen Accessioning and Processing (BAP)** Fax Supply Order Form (found in the Forms Packet) to the number listed on the form. Write the site address on the Fax Supply Order Form to where the supplies will be sent. There is no need to return unused kits to ~~MML~~ **BAP**.
- 14.251 Verify ALL sections of the Blood Specimen Submission Form, ~~MML~~ **BAP** Requisition Form, 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**. Do not send samples on weekends or holidays.
- 14.255 White bar-coded FedEx labels are affixed to the shipping boxes for shipment to ~~MML~~ **BAP**.
- 14.256 ~~MML~~ **BAP Receiving** will receive the samples and forward specimens immediately to the NCCTG Research Base Biospecimen Accessioning and Processing (BAP) laboratory, Stable 13-10A, Attention: BAP Supervisor.

Section 15.0**Drug Information**

Page 49-53:

Due to the receipt of the updated CAEPR for Sorafenib from NCI, Section 15.12 has been replaced in its entirety.

Pages 49-59:

Due to the inclusion of the updated Sorafenib CAEPR repagination has occurred.

Appendix I**Consent Form**

Page 9:

Due to the receipt of the updated CAEPR for Sorafenib from NCI, the risks have been updated as follows:

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

- Fatigue or tiredness
- Hair loss
- Inflammation of the skin on the palms of the hands or soles of the feet
- Loss of appetite
- ~~Rash/flaking or shedding of outer layer of skin~~ **Skin rash with the presence of macules (flat discolored area) and papules (raised bump) (reworded)**
- Diarrhea
- Nausea **or the urge to vomit** (*wording expanded*)
- Low levels of a blood protein called albumin
- Low blood phosphate level
- Stomach ache
- **Weight loss** (*moved from Less likely*)
- **High blood sugar** (*moved from Less likely*)
- **Decreased total number of white blood cells (leukocytes)** (*moved from Less likely and wording expanded*)
- **Decreased number of a type of white blood cell (lymphocyte)** (*moved from Less likely and wording expanded*)
- **High blood level of a liver pigment (bilirubin) indicative of abnormal liver function** (*moved from Less likely and wording expanded*)
- **Increased blood level of fat-digesting enzyme (lipase)** (*moved from Less likely and wording expanded*)
- **Decreased number of blood cells that help to clot blood (platelet)** (*moved from Less likely and wording expanded*)
- **Increased blood level of a liver enzyme (ALT/SGPT)** (*moved from Increased liver enzymes in Less likely and separated into individual entries*)
- **Increased blood level of a liver or bone enzyme (alkaline phosphatase)** (*moved from Increased liver enzymes in Less likely and separated into individual entries*)
- **Increased blood level of a liver enzyme (AST/SGOT)** (*moved from Increased liver enzymes in Less likely and separated into individual entries*)
- **Increased blood level of a digestive enzyme level (amylase)** (*moved from Less likely and reworded*)
- **Low blood calcium level** (*moved from Less likely*)
- **Low blood sodium level** (*moved from Less likely*)
- **Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)** (*newly added*)
- **Increased INR (measure of the ability of the blood to clot properly which increases the risk of bleeding)** (*newly added*)

Less Likely (events occurring less than or equal to 20% of the time)

- ~~Decrease in a red blood cell protein that carries oxygen in the body (deleted)~~
- ~~Nerve damage causing numbness, tingling, or burning~~ **Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning (reworded)**
- ~~Hoarseness, laryngitis, loss or change in voice (separated into individual entries below)~~
- **Irritation or sores in the lining of the voice box (separated from entry above)**
- **Irritation or sores in the lining of the throat (separated from entry above)**
- **Irritation or sores in the lining of the windpipe (separated from entry above)**
- **Voice change (separated from entry above)**
- Constipation
- Dry skin
- Fever
- ~~Weight loss (moved to Likely)~~
- ~~Abnormal liver or bone enzyme levels~~ **Increased blood level of a liver enzyme (GGT) (reworded)**
- ~~Kidney failure (deleted)~~
- ~~High blood sugar (moved to Likely)~~
- Low blood sugar
- High blood pressure
- Itching
- ~~Decreased total number of white blood cells (moved to Likely and wording expanded)~~
- ~~Decreased number of a type of white blood cell (move to Likely and wording expanded)~~
- Vomiting
- Pain (such as in the joints, muscles, headache, legs **and/or arms**, chest (**not heart related**), back, **bone**) (*additional risks added*)
- ~~Pain (deleted)~~
- ~~Allergic reactions (deleted)~~
- Bleeding in the reproductive organs or urinary system such as the bladder or kidney
- Fever with a dangerously low white blood cell count (**neutrophils**) (*wording expanded*)
- Infection with or without a low white blood cell count
- ~~Abnormal digestive enzyme level (moved to Likely and reworded)~~
- ~~High blood levels of a liver pigment indicative of abnormal liver function (moved to Likely and wording expanded)~~
- ~~Abnormal level of fat digesting enzyme (moved to Likely and wording expanded)~~
- ~~Decreased number of blood cells that help to clot blood (moved to Likely and wording expanded)~~
- Difficulty sleeping or falling asleep
- ~~Painful inflammation and ulceration of the lining of the digestive tract (deleted)~~
- Bleeding in the digestive tract
- Bleeding of the respiratory tract
- Swelling of the arms and legs
- ~~Increased liver enzymes (moved to Likely and separated into individual entries)~~
- ~~Low blood calcium level (moved to Likely)~~
- High blood potassium level
- Low blood potassium level
- ~~Low blood sodium level (moved to Likely)~~

- Dizziness (or sensation of lightheadedness, unsteadiness, giddiness, spinning or rocking) (*wording expanded*)
- Cough
- Shortness of breath
- Formation or presence of a blood clot inside a blood vessel
- **Lack of enough red blood cells (anemia)** (*newly added*)
- **Irritation or sores in the lining of the anus** (*newly added*)
- **Fluid collection in the abdomen** (*newly added*)
- **Irritation or sores in the lining of the mouth** (*newly added*)
- **Irritation or sores in the lining of the rectum** (*newly added*)
- **Irritation or sores in the lining of the small bowel** (*newly added*)
- **Test that shows a problem in blood clotting** (*newly added*)
- **Increased blood level of cholesterol** (*newly added*)
- **Decreased blood level of carbon dioxide** (*newly added*)
- **Decreased number of a type of white blood cell (neutrophil/granulocyte)** (*newly added*)
- **Increased blood level of calcium** (*newly added*)
- **Increased blood level of sodium** (*newly added*)
- **Increased blood level of uric acid, a waste material from food digestion** (*newly added*)
- **Muscle spasms** (*newly added*)
- **Sudden or traumatic injury to the kidney** (*newly added*)
- **Nose bleed** (*newly added*)

Rare but serious (events occurring less than 2% of the time)

- ~~Decreased blood supply to the heart~~ (*deleted*)
- Heart attack **caused by a blockage of a blood vessel supplying part of the heart** (*wording expanded*)
- Decrease in the ability of the heart to pump blood **during the “active” phase of the heartbeat (systole)** (*wording expanded*)
- A hole ~~somewhere in the intestinal tract from the esophagus to the anus~~ **in a part(s) of the digestive tract** (*reworded*)
- Bleeding into the brain or spinal cord
- Syndrome caused by high blood pressure characterized by headache, confusion, seizures, and vision loss associated with imaging findings
- **Collection of signs and symptoms that indicate sudden heart disease in which the heart does not get enough oxygen. Sudden symptoms such as chest pain, shortness of breath, or fainting could indicate heart disease and should be reported right away. Signs such as abnormal EKG and blood tests can confirm damage to the heart.** (*newly added*)
- **Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness** (*newly added*)
- **Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue** (*newly added*)
- **Potentially life-threatening condition affecting less than 10% of the skin in which cell death causes the epidermis (outer layer) to separate from the dermis (middle layer)** (*newly added*)