

North Central Cancer Treatment Group

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

Addendum 2 – March 7, 2008

**Summary**

- The Investigator Brochure (IB), Version date October 18, 2007, for Pemetrexed has been received. The consent form risks and drug information section have been updated accordingly.
- Clarification to blood pressure monitoring in the consent form.
- Editorial/administrative changes.

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

**Title page** Updated to reflect Addendum 2 and revised NCI version date.

**Protocol Resource**

Page 2: **Rachael M. Meyers** replaces ~~Jennifer P. Schreiber~~ as the NCCTG *Research Base* Quality Control Specialist.

**Schema**

Page 4: A footnote has been added to observation for clarification as follows:  
**\*\*\* The observation phase is only 1 cycle for data entry purposes, no matter how long the patient stays in observation.**

**Section 4.0**

Page 19: **Test Schedule**  
A comma has been added between phosphatase and lipase for clarification.

**Section 15.0**

Page 55: **Drug Information**  
Section 15.192 has been revised for consistency with the protocol and package insert as follows:

**Sorafenib should be taken on an empty stomach** ~~Drug should be taken~~ with at least 250 cc of water. ~~May be taken with or without food.~~ Do not administer with grapefruit juice.

Page 57: Due to the receipt of the updated IB for pemetrexed, **“Mouth ulcers”** has been added to the “Very common” category in Section 15.23.

**Appendix I**

Page 3:

**Consent Form**

The seventh paragraph under the “During the study” section has been revised as follows for clarification of the blood pressure monitoring:

If two systolic readings (the top reading of the blood pressure value) in a row on ~~two different days~~ **the same day (at least 1 hour apart)** are greater than or equal to 140 mmHg OR two diastolic readings (the bottom reading of the blood pressure value) in a row on ~~two different days~~ **the same day (at least 1 hour apart)** are greater than or equal to 90 mmHg, you should contact your study doctor or local doctor as soon as possible. You should contact your study doctor or local doctor at any time if the top blood pressure reading is greater than 150 mmHg or if your bottom blood pressure reading is greater than 100 mmHg. Also, contact your study doctor or local doctor if you think you are having any signs (for example, headaches) that might lead you to think your blood pressure is too high.

Pages 10-11:

Due to the receipt of the updated IB for pemetrexed, the risks section of the consent form has been revised as follows:

**Likely risks of Pemetrexed (Alimta) (events that occur greater than 20% of time)**

- ~~Fall in the number of white blood cells and red blood cells. The bone marrow makes the white blood cells, red blood cells, and platelets. A fall in the white blood cells leads to a risk of getting an infection. A fall in the red blood cells may lead to anemia with feelings of being tired and loss of energy. (Split into two separate entries below)~~
- **Low white blood cells which may lead to infection**
- **Low red blood cells which may lead to fatigue and/or less energy**
- Nausea - Feeling sick to the stomach
- Vomiting - Throwing up
- Diarrhea - Loose stools
- Loss of body fluids (dehydration which may require intravenous fluids)
- Loss of appetite
- ~~Less energy (deleted)~~
- Mild hair loss (**alopecia**) (*expanded wording*)
- Itchy skin rash
- Shortness of breath
- Abdominal (**stomach**) pain (*expanded wording*)
- Weakness
- Constipation (**irregular or difficulty in passing stool**) (*expanded wording*)
- Fever
- **Mouth ulcers (similar to canker sores)** (*moved from “Less Likely” category*)

**Less Likely risks of Pemetrexed (Alimta) (events that occur less than or equal to 20% of time)**

- Fall in the platelet count that may lead to the risk of bruising and bleeding after an injury.
- Infection in the blood with fever (caused by a fall in the number of white blood cells)

- Change in liver chemistry, which may end in high liver function tests (tests that show how the liver is working) (*reworded*)
- ~~Fall~~ **Decrease** in kidney function (*reworded*)
- Mouth ulcers (similar to canker sores) (*moved to “Likely” category*)
- Inflammation (swelling, redness, pain) of the skin
- Infection such as urinary tract infection
- Blood clots
- Burning, itchy, red sore eyes with lots of watering
- Increase in body fluids (swelling, **edema**) (*expanded wording*)
- Sores on the skin or local redness, pain, and/or swelling at the site of the injection

**Rare but serious risks of Pemetrexed (Alimta) (events that occur less than 2-3% of time)**

- Allergic reaction
- Abnormal heart rhythm

~~Depending on the result of your kidney tests, your study doctor may not let you take aspirin or aspirin-like drugs~~ **You should not take aspirin or aspirin-like drugs** (i.e., Ibuprofen, Advil®, Motrin®, Aleve®, etc.) (NSAIDS) ~~up to 10~~ **for two days before getting treatment, on the day of treatment, and for two days and after getting** treatment with pemetrexed. Aspirin and aspirin-like drugs can cause trouble with your ability of passing pemetrexed through your body, raising the risk of low blood counts that can lead to infections and bleeding. Tylenol, however, may be used.

**Appendix V**

Page 1:

The following has been added to #3 for clarification:

Isolate CTCs from two EDTA tubes at the indicated time points using the protocol entitled “Isolation of Circulating Tumor Cells” (**Dynabead method**)...