

North Central Cancer Treatment Group

N0321: Phase I/II Study of PS-341 in Combination with Paclitaxel, Carboplatin, and Concurrent Thoracic Radiation Therapy for Non-small Cell Lung Cancer (NSCLC)

Addendum 6 – June 8, 2007

**Summary**

- The 9<sup>th</sup> edition of the investigator brochure dated July 26, 2006 for PS341 has been received. Therefore, the drug information section and the risks section of the consent forms have been revised accordingly.
- Editorial/administrative changes.

**A replacement protocol is provided. Please replace the current copy with the one attached. Please keep this addendum with your protocol.**

**Title page** Updated to reflect Addendum 6 and revised NCI version date.

**Protocol Resource Page**

Page 2: The title and e-mail address have been corrected for Vicki Bryhn as follows:  
NCCTG Research Base Protocol Administration ~~and~~ve Specialist  
[bryhn.vicki@mayo.edu](mailto:bryhn.vicki@mayo.edu)

Section 15.0 Drug Information

Page 42: Due to the receipt of an updated investigator brochure (IB) for PS341, the following risks have been added at the bottom of Section 15.16:

**Due to IB review: Inflammation in the peripheral blood vessels with bleeding into the brain; changes in heart rate or rhythm.**

**Appendices IA and IB Consent Forms**

Pages 5-8: Due to the receipt of an updated IB for PS341, the “What are the risks of the study?” section of the consent form has been revised as follows:

**Likely related side effects of PS-341 (events occurring greater than 20% of the time):**

- Fatigue (feeling tired or weak); **lethargy, malaise** (*expanded wording*)
- Loss of appetite
- **Weight loss** (*moved from Less Likely due to IB review*)
- Nausea (feeling sick to your stomach)
- Vomiting (throwing up)
- Pain – Abdominal ~~stomach~~ (*moved from Less Likely due to IB review*), headache/**head** (*expanded wording added that was in the CAEPR previously but not in the consent*), **bone, joints** (*moved from Less Likely due to IB review*)
- Pain or swelling in the arms or legs (*moved from Less Likely due to IB review*)
- Weakness caused by damage of the nerves (*moved from Less Likely due to IB review*)
- Diarrhea

- Constipation (difficulty passing stool)
- Fever
- Lowering of the red blood cell count causing anemia
- Lowering of blood clotting cells with an increased risk of bleeding **and may lead to life-threatening bleeding** (*expanded wording*)
- Lowering of the white blood cell counts with an increased risk of infection **and even life-threatening infections** (*category changed due to IB review plus expanded wording*)
- Problems with the central nervous system (the brain and spinal cord) which controls mental activities, movements and nerves
- **Dehydration - Loss of fluid in the body, may need to stay in the hospital** (*rewording and moved from Less Likely due to IB review*)
- ~~Neurologic effects such as~~ Numbness, tingling or weakness in the arms and legs (**neuropathy**) (*rewording due to IB review*)
- **Feeling dizzy or lightheaded** (*moved from Less Likely due to IB review*)
- **Anxiety** (*previously in CAEPR but not in consent and category changed to Likely due to IB review*)
- **Cough** (*moved from Less Likely due to IB review*)
- Shortness of breath
- **Rash** (*moved from Less Likely due to IB review*)
- **Low blood pressure** (*moved from Less Likely due to IB review*)
- **Decrease in kidney function, kidney damage or failure** (*moved from Less Likely due to IB review*)
- **Pneumonia** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)
- **Irritation in the stomach or intestinal tract** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)

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Less likely related side effects of PS-341 (*events occurring greater than 3% but less than 20% of the time*):

- Runny, stuffy, or itchy nose
- Ringing or buzzing in the ears
- ~~Lowering of the white blood cell counts with an increased risk of infection~~ (*moved to Likely due to IB review*)
- ~~Low blood pressure~~ (*moved to Likely due to IB review*)
- Drop in heart's ability to pump blood
- Fluid around the heart
- Trouble sleeping
- Uncontrollable shaking and chills
- ~~Weight loss~~ (*moved to Likely due to IB review*)
- Redness in the face
- Bruising, bleeding, soreness or redness of the skin where the injection is given
- Itching
- ~~Rash~~ (*moved to Likely due to IB review*)
- **Skin peeling** (*originally in the CAEPR but not in the consent*)
- Hives or welts on the skin
- ~~Loss of fluid in the body, may need to stay in the hospital~~ (*moved to Likely due to IB review*)
- Passing gas
- Heartburn

- Slowing of the small intestine causing stomach pain, bloating and cramping (**ileus**) (*expanded wording*)
- Sores in the lining of the throat
- Changes in taste
- Bleeding anywhere in the body (**i.e., intestine, brain**) (*expanded wording due to IB review*)
- Fever with low white blood cell count
- Infection (sinus)
- Swelling in the head and neck
- ~~Swelling in the arms or legs~~ (*moved to Likely due to IB review*)
- Abnormal tests of liver function
- ~~Decrease in kidney function, kidney damage or failure~~ (*moved to Likely due to IB review*)
- High/low blood sugar
- **Increase or decrease in critical salts from the blood including sodium, potassium, magnesium, phosphate, calcium** (*rewording due to IB review*)
- ~~Low magnesium, phosphate, sodium, levels in the blood~~ (*reworded and included in bullet just above*)
- ~~Low phosphate levels in the blood~~ (*reworded and included in bullet just above*)
- Change in walking stride or function (walking with a limp)
- ~~Feeling dizzy or lightheaded~~ (*moved to Likely due to IB review*)
- Mood changes (feeling agitated)
- ~~Weakness caused by damage of the nerves~~ (*moved to Likely due to IB review*)
- Fainting
- Dry eye syndrome
- Damage to the surface of the eye
- Double or blurred vision
- Pain in the back, ~~bones~~ (*moved to Likely category due to IB review*), chest, ~~arms, legs, joints~~ (*moved to Likely category due to IB review*), muscles, throat, voice box, ~~stomach~~ (*moved to Likely category due to IB review*), or nerves
- ~~Cough~~ (*moved to Likely due to IB review*)
- Hiccups
- Fluid around the lungs
- **Potentially life threatening allergic reaction to the medication** (*rewording and moved from statement below Rare but serious category*)
- **Changes in heart rate or rhythm** (*new added due to IB review*)
- **New onset of heart failure** (*originally in the CAEPR but not in the consent*)
- **Sepsis (severe infection which could lead to multi-organ dysfunction or death)** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)
- **Inflammation of the pancreas** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)
- **Inflammation in the intestinal tract** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)
- **Severe nerve damage resulting in profound weakness, paralysis, confusion, or seizures** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)

Rare but serious side effects of PS-341:

- Abnormal hole in the GI tract
- **Difficulty with urinating** (*originally in the CAEPR under undetermined but not in the consent and now the category has changed due to IB review*)
- **Inflammation in the peripheral blood vessels with bleeding into the brain** (*newly added due to IB review*)

~~As with any medication, allergic reactions are a possibility.~~ (*moved to Less Likely due to IB review*)