

North Central Cancer Treatment Group

N0543: A Phase II Trial of Pharmacogenetic-Based Dosing of Irinotecan, Oxaliplatin, and Capecitabine as First-Line Therapy for Advanced Small Bowel Adenocarcinoma

Addendum 4 – July 11, 2008

**Summary**

- Section 15.0 and consent form changes based on Irinotecan Package Insert, dated 03/26/2008
- Administrative/Editorial Changes.

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

**Title page** Title page has been revised to include Addendum 4 and a new NCI version date.

**Protocol Resource Page**

Page 2: Contact information have been revised for the “Paraffin-embedded tissue pathology contact as follows:

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The fax number for Jacqueline Lafky has been revised.

**Section 15.0 Drug Information**

Page 46: The following risks have been added at the end of Section 15.16 due to revised Irinotecan Package Insert, dated 03/26/2008:

**The following risks have been reported in the Irinotecan Package Insert: general discomfort, constipation, anorexia, excessive salivation, pancreatitis, and bradycardia.**

**Appendix I Informed Consent**

Pages 7-8: Based on Irinotecan (CPT-11) package insert, dated 03/26/2008, the following text has been revised:

**Likely risks of Irinotecan (CPT-11) (events occurring greater than 20% of the time)** *(new per package insert review)*

- Diarrhea (loose stools). If diarrhea happens, it may be very bad. There are two kinds of diarrhea that can happen:
  - Early diarrhea may happen within 8 hours of when you get your chemotherapy. Before it happens, you might have cramps in your stomach, teary eyes, and sweating. If you get diarrhea within an hour after getting irinotecan, you may get a drug called atropine through a vein in your arm.
  - Late diarrhea may happen more than 8 hours after your chemotherapy. It can lead to dehydration (loss of water and body fluids from the body) and changes in the levels of some of the chemicals in your body. Late diarrhea can be life-threatening. You will take a drug called loperamide as soon as the loose stools start or when you have more stools than normal. Loperamide will help stop the diarrhea.

If you get diarrhea, you should call your doctor right away. You will need to keep track of when the loose stools start, how often they happen, and how many loose stools you have. If the diarrhea does not get better, you may need to go into the hospital.

- ~~Lowering of the white blood cell count red blood cell or platelet counts in your blood. This can lead to anemia and~~ *(risks separated below)* **that can lead to a higher risk of infection and bleeding** *(part of platelet risk below)* ~~It is especially bad if loose stools happen at the same time that the white blood cell, red blood cell, or platelet count is low. There have been deaths reported when these two side effects have happened together. Although the risk of death is low, this shows you how important it is to call the doctor or nurse about any side effects you are having.~~ *(last three sentences moved to "rare but serious" per package*

*serious” per package insert)*

- **Low red blood cell count (anemia) that may make you feel tired and short of breath, a transfusion may be needed** (*this risk has been separated from above and revised per package insert*)
- **Low platelet count (thrombocytopenia) that may lead to bleeding or easy bruising** (*this risk has been separated from above and revised per package insert*)
- Nausea (feeling sick to your stomach)
- Vomiting (throwing up)
- ~~Fatigue (tiredness)~~ (*moved to “less likely” per package insert*)
- Hair loss
- ~~Fever and chills~~ (*moved to “less likely” per package insert*)
- ~~Flushing~~ (*moved to “less likely” per package insert*)
- ~~Low blood pressure~~ (*moved to “less likely” per package insert*)
- Tightness in the chest
- Back pain
- Sleeplessness
- Dizziness
- ~~Irritation of the area where the irinotecan is injected~~ (*moved to “less likely” per package insert*)
- **Sore mouth** (*moved from “rare, but serious” per package insert review*)
- ~~Non-productive Cough~~ (*moved from “rare, but serious” with ‘non productive’ removed per package insert review*)
- **Trouble breathing, shortness of breath. In some cases; this has resulted in death.** (*moved from “less likely” per package insert review*)
- **Sores (ulcers) of the bowels** (*new per package insert review*)
- **Trouble passing stool (constipation)** (*new per package insert review*)
- **Loss of appetite** (*new per package insert review*)
- **General discomfort** (*new per package insert review*)

**Less Likely risks of Irinotecan (CPT-11) (events occurring less than or equal to 20% of the time)** (*new per package insert review*)

- ~~Trouble breathing, shortness of breath. In some cases; this has resulted in death.~~ (*moved to “likely” per package insert review*)
- Weakness
- **Skin rash, may be with redness or itching** (*moved from “rare, but serious” per package insert review*)
- **Problems with liver or kidney function** (*moved from “rare, but serious” per package insert review*)
- **Heavy sweating** (*new per package insert review*)

- **Excessive moistness (saliva) of mouth** (*new per package insert review*)
- **Slower heart beat** (*new per package insert review*)
- **Watery eyes** (*new per package insert review*)
- **Fever and chills** (*moved from “likely” per package insert*)
- **Flushing or a warm sensation** (*moved from “likely” and revised per package insert*)
- **Low blood pressure, which may cause lightheadedness or dizziness, or may cause you to pass out** (*moved from “likely” and revised per package insert*)
- **Irritation of the area where the irinotecan is injected caused by leaking of the drug and may cause sores on the skin or very bad redness and soreness** (*moved from “likely” and revised per package insert*)
- **Fatigue (tiredness)** (*moved from “likely” per package insert*)

**Rare, but serious risks of Irinotecan (CPT-11) (events occurring less than 2-3% of the time)** (*new per package insert review*)

- ~~Moistness of mouth, sweating, stomach cramps, and diarrhea may occur~~ **During the time you are getting irinotecan or within 24 hours, the following may occur; Moistness of mouth, sweating, stomach cramps, and diarrhea may occur** (*reworded for clarity*)
- ~~Sore mouth and~~ **Changes in taste** (*Sore mouth moved to “likely” per package insert review*)
- ~~Skin rash, may be with redness or itching~~ (*moved to “less likely” per package insert review*)
- ~~Problems with liver or kidney function~~ (*moved to “likely” per package insert review*)
- ~~Non-productive cough~~ (*moved to “likely” per package insert review*)
- Nasal congestion or stuffiness
- Higher risk of developing blood clots
- **It is especially bad if loose stools happen at the same time that the white blood cell, red blood cell, or platelet count is low. There have been deaths reported when these two side effects have happened together. Although the risk of death is low, this shows you how important it is to call the doctor or nurse about any side effects you are having.** (*moved from “likely” per package insert review*)
- **Increased pancreas enzymes levels which can lead to pancreatitis, a condition where the pancreas becomes inflamed and can cause pain.** (*new per package insert review*)