

North Central Cancer Treatment Group

N0432 Phase II Trial of Docetaxel with Capecitabine and Bevacizumab as First-Line Chemotherapy for Patients with Metastatic Breast Cancer

Addendum 7 – March 9, 2007

Summary

- **Consent form risks updated to match current investigator’s brochures for docetaxel (Version 10), capecitabine (Version 8) and bevacizumab (Version 13, Add 1)**
- Administrative and editorial changes.

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

Title Page

- Document History is updated to reflect this addendum.
- NCI Version Date has been updated.

Section 10.0

Adverse Event (AE) Reporting and Monitoring

Pages 28-32: Repaginated so Table 10.3 is entirely on page 28. Section 11.0 moved to start on page 30 and repaginated across pages 30-32 to allow room for Section 10 expansion in future, if needed.

Appendix I

Consent Form

Page 1: Revision date updated to match NCI version date.
Pages 5-11: Repaginated due to added information on pages 5-8.
Page 5: Risks of docetaxel updated to correspond with current version of Investigator Brochure (Version 10). Changed headers to reflect frequency (e.g. *more than 20%*).

Under Docetaxel ~~Common Side Effects~~ Likely Risks (occurring >20% of the time)

Edited “Lowering of blood counts” to delete ~~risk of bleeding~~ and moved to *Less Likely* and edited to read “Lowering of platelets in the blood that may lead to bleeding problems”

Edited “Feeling sick to the stomach” to add **(nausea)** and **(vomiting)**

Edited “Loose stools” to add **(diarrhea)**

Edited “Lack of energy” to add **tiredness and/or general weakness**

Edited “Sleepiness” to add **Unusual**

Edited “Loss of taste” to add **or change in taste**

Edited “Loss of appetite (not feeling hungry, not wanting to eat)” to add **and/or weight loss**

Page 5:

Edited “Muscle aches” to add **or joint pain**

Moved “Swelling of legs and feet” to *Less Likely*

Added the following new risks under docetaxel *Likely*:

- **Shortness of breath**
- **Irritation (sore, itchy) skin or loss of skin on hands or soles of feet**

Under Docetaxel ~~Less Common Side Effects~~ **Likely Risks (occurring ≤20% of the time)**

Edited “Liver damage” to Liver **problems (may have yellowing of skin and eyes)**

Edited “Allergic reactions” to add **or low back pain**

Moved “Nerve damage (numbness and tingling) – usually but not always reversible” to *Likely* and edited to read “Nerve damage – **loss of feeling or numbness and tingling in fingers and toes**”

Moved “Lung damage (may cause breathing problems)” to *Rare but Serious* and edited to read “Lung problems – **inflammation of the lungs which may cause shortness of breath, cough and/or fever**”

Added the following risks under docetaxel *Less Likely*:

- **Too much fluid around the lungs and heart (may feel short of breath)**
- **Tiredness and/or pain in upper right belly**
- **Rash, redness and/or swelling of the skin**
- **Vasculitis –inflammation of the veins that may cause itching or swelling in arms or legs**
- **Seizures**

Deleted the following risks under docetaxel *Likely*:

- ~~Fingernail or toenail loss~~

Under Docetaxel ~~Rare but Serious Side Effects~~ **Risks (occurring <2-3% of the time)**

Edited Liver failure to delete (~~may require liver transplant~~) since the patient would not be eligible for liver transplant.

Moved “Irregular heartbeat” to *Less Likely*

Added the following new risks under docetaxel *Rare but Serious*:

- **Death**

Deleted the following risks under docetaxel *Rare but Serious* (as their frequency and association with docetaxel has dropped with the new IB):

- ~~Bowel irritation~~
- ~~Severe allergic reactions with changes in blood pressure and shortness of breath~~
- ~~Severe skin reactions including shedding of skin or skin redness~~

Page 5: Added the following language below the table of docetaxel risks:
The following side effects have been reported for patients taking part in other docetaxel (Taxotere®) research studies. It is not known if these side effects were related to the docetaxel

- **Heart Failure**
- **Low or high blood pressure**
- **Hearing problems**
- **Kidney failure**

Page 6: Risks of capecitabine updated to correspond with current version of Investigator Brochure (Version 8). Changed headers to reflect frequency categories (e.g. *more than 20%*)

UNDER Capecitabine - Likely Side Effects (*happen more than 20% of the time*)

Edited Diarrhea to include “**(loose stools)**”

Edited Nausea to include “**(feeling sick to your stomach)**”

Edited Sores and swelling in the mouth to include “**and throat**”

Added risk: **Dry or itchy skin**

Moved Vomiting to *Less Likely*

Moved Stomach pain to *Less Likely* and added “**or abdominal**”

Moved Constipation to *Less Likely* and added “**(hard stools or trouble passing stool)**”

Moved Tiredness, feeling run down to *Less Likely* and revised to read “**Fatigue** (feeling tired, run down)”

Moved Skin rash to *Less Likely*

UNDER Capecitabine – ~~Less Likely but Serious~~ Side Effects (*happen less than or equal to 20% of the time*)

Added new risks under *Less Likely Side Effects*:

- **Heartburn**
- **Weakness, loss of energy, loss of interest in activities**
- **Hair loss**
- **Rash**
- **Fever**
- **Infection**

Moved “Dehydration – loss of water in the body that can lead to hospitalization to *Rare but Serious* and added “severe”.

Moved “Problems with liver function (as seen on a blood test) to *Rare but Serious* and edited to include **liver failure**.

Deleted risks under capecitabine *Likely* and *Less Likely*:

- ~~Edema~~
- ~~Shortness of Breath~~

Page 6: Added category below table for capecitabine ***Rare but serious risks of capecitabine (events occurring less than 2-3% of the time)*** with ***new*** risks of:

- **Blood clots and/or bleeding**
- **Heart attack**
- **Abnormal heart rhythm**

Page 7: Risks of bevacizumab updated to correspond with current version of Investigator Brochure (Version 13). Changed headers from “common” to “likely” and added info to reflect frequency categories (e.g. *events that occur >20%*)

Under bevacizumab ~~Less Common~~ **Likely Risks (event that occur ≤20%)**

Edited Inflammation (swelling, redness) of the lining of the mouth and/or throat to include “or sores”

Moved Bowel perforation from *Rare* to *Less Likely*

Added ***new*** risks under bevacizumab *Less Likely*

- **Fistula (an opening in the bowel that connects dying tumor to nearby bowel and may require surgery to repair)**
- **Coughing up blood**
- **Voice changes**

Added ***new*** risks under bevacizumab ***Rare but Serious Side Effects Risks (events that occur <2-3% of the time):***

- **Heart attack**
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS) - see below for description**

Page 8: Added paragraph below table of bevacizumab risks and relabeled next section.

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

- **Lowered white blood cells (may make you more likely to get infections and fever may also be present)**
- **Decrease in blood salts such as potassium or phosphorous (seen on a blood test)**
- **Increase in blood sugar (seen on a blood test)**
- **Abnormalities in liver function tests (type of blood test that may lead to liver problems)**

Additional risks of Bevacizumab...