



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Operations Office

Date: January 7, 2011
To: Primary Clinical Research Associates
From: Lynn Flickinger
Re: N083E, Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in Early Breast Cancer

Attached are updated forms for this protocol. Edits are as follows:

CRF Title	Brief Description of Edit
Nadir/Adverse Event Form	<ul style="list-style-type: none">Added "CTCAE v3.0" to CTC Adverse Event Term on all pages.
Baseline Adverse Events Form	<ul style="list-style-type: none">Added "CTCAE v3.0" to CTC Adverse Event Term.

If you have any questions, please contact Lynn Flickinger (flickinger.lynn@mayo.edu or telephone at 507-538-7035).

Attachments

North Central Cancer Treatment Group

N083E, Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in Early Breast Cancer

Addendum 4 – January 7, 2011

Summary

- In compliance with the NCI/CTEP mandate (dated May 28, 2010), expedited adverse event reporting requirements were converted from CTCAE v3.0 to CTCAE v4.0 (affected sections 10.1 and 10.11) while routine data collection via Case Report Forms (which includes the Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form) will remain using CTCAE v3.0 (clarifications added to sections 8.2, 8.3, 8.6, 10.22, 10.3, and 10.31). Effective April 1, 2011, expedited reporting via AdEERS must use CTCAE v4.0 while the remainder of the data collection for legacy trials will continue to use CTCAE v3.0.
- Per NCI, the Secondary AML/MDS Report Form will no longer be used. Therefore, Sections 10 and 18 have been revised accordingly.

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

Title page: Updated to reflect Addendum 4 and the NCI version date.

Section 8.0 **Dosage Modification Based on Adverse Events**
 Pages 24-26: The first column headers in Sections 8.2 and 8.3 tables have been revised for clarification as follows:

CTCAE v3.0 CATEGORY

Section 10.0 **Adverse Event (AE) Reporting and Monitoring**
 Page 35: Section 10.1 and Section 10.11 have been revised as follows to update the required AE reporting from CTCAE v3.0 to CTCAE v4.0:

~~This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 for adverse event (AE) monitoring and reporting. The CTCAE v3.0 can be accessed from the CTEP home page (<http://ctep.cancer.gov>).~~
CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 will be utilized until March 31, 2010. CTCAE version 4.0 will be utilized for expedited adverse event reporting only, beginning April 1, 2011. All appropriate treatment areas should have access to a copy of the CTCAE v3.0. **A copy of the CTCAE version 4.0 can be downloaded from the CTEP web site (<http://ctep.cancer.gov>).**

10.11 Adverse event monitoring and reporting is a routine part of every clinical trial...

Expedited adverse event reporting requires submission of an Adverse Event Expedited Reporting System (AdEERS)...

Effective with Addendum 4, and beginning April 1, 2011, expedited AdEERS reporting for this protocol has been updated by the NCI/CTEP to use CTCAE v4.0. Therefore;

- 1) **Events requiring expedited reporting through AdEERS must be reported through the AdEERS system in CTCAE v4.0.**
- 2) **The events reported via AdEERS must ALSO be reported through routine reporting (i.e., Case Report Forms) using CTCAE v3.0.**
- 3) **Routine data collection via Case Report Forms, including the “Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form,” will remain using CTCAE v3.0 for this study.**

Page 36:

Due to the removal of the Secondary AML/MDS Report Form, a new third bullet has been added under the table in Section 10.21 as follows:

- **SECONDARY MALIGNANCIES (defined as “cancer caused by treatment for a previous malignancy,” e.g., treatment with radiation or chemotherapy) are to be reported through AdEERS, as noted in Section 10.22. Secondary malignancies are not considered metastasis of the initial neoplasm. Secondary malignancy is unrelated to the first cancer that was treated, and may occur months or even years after initial treatment.**

Note: Second Primary malignancy (malignancy not due to prior treatment) should not be reported through AdEERS.

The second bullet under the Additional Instructions section in Section 10.21 has been updated to reflect current submission procedures as follows:

In the rare event when Internet connectivity is disrupted, ~~a report may be prepared using the Adverse Event Expedited Report—Single Agent or Multiple Agents paper template (available on the CTEP Home Page at <http://ctep.cancer.gov>) and faxed to 301-230-0159. Contact the NCCTG SAE Coordinator (as identified on the NCCTG Protocol Resources page) for additional back-up submission instructions~~ **24-hour notification is to be made to NCI by telephone at: 301-897-7497. An electronic report MUST be submitted immediately upon re-establishment of internet connection. Please note that all paper AdEERS forms have been removed from the CTEP web site and will NO LONGER be accepted.**

Page 37: Due to the removal of the Secondary AML/MDS Report Form, the second column for the “Secondary AML/MDS” section has been revised as follows:

Reporting for this event required during and after completion of study treatment **via AdEERS**.

Through March 31, 2011, continue using CTCAE v3.0: Report Myelodysplasia as “Blood/Bone Marrow – Myelodysplasia” and Leukemias as “Blood/Bone Marrow – Other (Specify, _____).”

Beginning April 1, 2011, AdEERS will only accept CTCAE v4.0 for this study. Report these events using “Neoplasms benign, malignant and unspecified (incl. cysts and polyps)” and including the appropriate adverse event:

- Leukemia secondary to oncology chemotherapy OR
- Myelodysplastic syndrome OR
- Treatment related secondary malignancy

~~Submit the NCI/CTEP Secondary AML/MDS Report form within 15 days via fax or mail to the NCCTG SAE Coordinator, NCCTG Operations Office, 200 First Street SW, Rochester, MN 55905, Fax (507)284-9628. The Operations Office will submit to NCI.~~

The second column for “Other Grade 4 or 5 Events...” section in Section 10.22 has been revised for clarification as follows:

Complete a Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form within 5 working days, **using CTCAE v3.0**.

If an AdEERS report has been submitted, this form does not need to be submitted.

You must use CTCAE v3.0 for data submission with this form. The events reported on this form must also appear on the Case Report Forms (i.e., routine data) for this study.

Submit the Non-AER form electronically via the NCCTG Remote Data Entry System within 5 working days of the date the CRA is aware of the event(s) necessitating the form.

The NCCTG SAE Coordinator will notify the NCCTG IND Coordinator who will submit to the FDA IND as warranted by the event and stipulated in the U.S. Code of Federal Regulations.

Pages 38-39: Section 10.3 and Section 10.31 have been revised for clarification. In Section 10.3, the first column header in the table has added **(CTCAE v3.0)** and Section 10.31 has been revised as follows:

Submit to the NCCTG Research Base via the Nadir/AE Log the following AEs **using CTCAE v3.0** experienced by a patient and not specified in Section 10.3:

Section 18.0 Records and Data Collection Procedures

Page 72: With the removal of the Secondary AML/MDS Report Form, the row for the “NCI/CTEP Secondary AML/MDS Report Form” has been deleted. Secondary AML/MDS is now reported through AdEERS, see Section 10.22).

North Central Cancer Treatment Group

Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in
Early Breast Cancer

*For any communications regarding this protocol,
please call the protocol resource person on the following page.*

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Statistician: David W Hillman MS[√]
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Drug Availability

DCTD Supplied Investigational Agents: None

Commercial Agents: docetaxel, carboplatin, trastuzumab

Drug Company Supplied: lapatinib (NSC 727989) – IND exempt

***Investigator having NCI responsibility for this protocol**

[√]Study contributor(s) not responsible for patient care

Document History	(Effective Date)
Activation	20 February 2009
Addendum 1	August 14, 2009
Addendum 2	September 25, 2009
Addendum 3	May 14, 2010
Addendum 4	January 7, 2011

<u>Study Participants</u>	<u>Date Activated</u>
Entire NCCTG	20 February 2009

NCI Version Date: December 16, 2010

Table 8.2 Dose Modifications Based on Interval Adverse Events (Other than Day 1)

Add 4

CTCAE v3.0 CATEGORY	ADVERSE EVENT	AGENT	ACTION
Cardiac General	Decline in LVEF below 50%	lapatinib trastuzumab	See Section 8.5 Cardiac Assessment
Dermatology/ Skin Gastrointestinal	Rash: acneiform Grade 2	lapatinib	See Section 8.6 for Dermatologic Assessment
	Diarrhea	carboplatin docetaxel lapatinib	See Section 8.7 Algorithm for Diarrhea Management and Section 9.0 for specific recommendations
Metabolic/ Laboratory	ALT, SGPT (serum glutamic pyruvic transaminase) Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4
	≥Grade 3		Discontinue lapatinib permanently
	AST, SGOT (serum glutamic oxaloacetic transaminase) Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4
	≥Grade 3		Discontinue lapatinib permanently
	Bilirubin Total bilirubin >ULN Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4
	≥Grade 3		Discontinue lapatinib permanently
Pulmonary	Interstitial pneumonitis, adult respiratory distress syndrome (ARDS), or non-cardiogenic pulmonary edema. Grade 3 or 4 pneumonitis/fibrosis or pulmonary infiltrate is confirmed.	lapatinib trastuzumab	Omit lapatinib and trastuzumab therapy (for up to 3 weeks) All incidences of interstitial lung disease/ interstitial pneumonitis regardless of grade must be reported as serious adverse events (SAEs)
Other non-hematologic adverse events	Grade 3	docetaxel carboplatin lapatinib trastuzumab	Omit or hold appropriate drug(s) until ≤Grade 2, then retreat ↓ one dose level
	Grade 4		Discontinue appropriate drug(s)

8.3 Dose Modifications at Time of Retreatment (Day 1 of subsequent cycles)

Add 4

CTCAE v3.0 CATEGORY	ADVERSE EVENT	AGENT	DOSAGE CHANGE
Allergy/ Immunology	Allergic reaction/ hypersensitivity (including drug fever)* Grade 1	carboplatin docetaxel	Complete infusion at initial planned rate (see Section 9.81)
	Grade 2		Interrupt infusion (see Section 9.82)
	Grade 3		Immediately discontinue infusion (see Section 9.83)
	Grade 4		Immediately discontinue infusion Discontinue treatment
Blood/Bone Marrow	Neutrophils/granulocytes (ANC/AGC) ≥Grade 2 neutropenia ANC <1500/mm ³	carboplatin docetaxel	Hold chemotherapy and trastuzumab until ANC ≥1500 If not recovered by Day 21, discontinue treatment.
	Platelets ≥Grade 2 thrombocytopenia or PLT <75,000/mm ³	carboplatin docetaxel	Hold chemotherapy and trastuzumab until platelets ≥100,000 If not recovered by Day 21, discontinue treatment
Cardiac General Constitutional Symptoms	Decline in LVEF	lapatinib trastuzumab	See Section 8.6 Cardiac Assessment
	Fatigue (lethargy, malaise, asthenia) Grade 2	carboplatin docetaxel	↓ 1 dose level and continue treatment
	≥Grade 3	carboplatin docetaxel	↓ 1 dose level and continue treatment If not ≤Grade 2 in 14 days, discontinue treatment
Dermatology/ Skin	Rash: hand-foot skin reaction Grade 1	docetaxel	Continue treatment on schedule, treat symptomatically
	Grade 2		↓ 1 dose level and continue treatment
	Grade 3		↓ 1 dose level and continue treatment If not ≤Grade 2 in 14 days, discontinue treatment
	Rash: acneiform ≥Grade 2	lapatinib	See Section 8.6 Dermatologic Assessment
Gastrointestinal	Diarrhea	carboplatin docetaxel lapatinib	See Section 8.7 Algorithm for Diarrhea Management and Section 9 for specific recommendations
	Mucositis/stomatitis (clinical exam) - Oral cavity - Pharynx ≥Grade 3	docetaxel	Hold all treatment (for maximum of one cycle/21 days) until ≤Grade 1, then ↓ 1 dose level
Infection	Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC <1.0x 10 ⁹ /L, fever ≥38.5°C) Grade 3 or 4	carboplatin docetaxel	Hold all treatment (for maximum of one cycle/21 days) until symptoms resolve then ↓ 1 dose level of each agent in subsequent cycles

Add 1

Add 1

Add 4

CTCAE v3.0 CATEGORY	ADVERSE EVENT	AGENT	DOSAGE CHANGE
	Infection with normal ANC or Grade 1 or 2 neutrophils - Lung (pneumonia) Grade 4	carboplatin docetaxel	Hold all treatment (for maximum of one cycle/21 days) until symptoms resolve then ↓ 1 dose level of each agent in subsequent cycles
Metabolic/ Laboratory	Alkaline phosphatase	docetaxel	See Table 8.4 for dose modifications for docetaxel for abnormal liver function
	ALT, SGPT (serum glutamic pyruvic transaminase)	docetaxel	See Table 8.4 for dose modifications for docetaxel for abnormal liver function
	AST, SGOT (serum glutamic oxaloacetic transaminase)	docetaxel	See Table 8.4 for dose modifications for docetaxel for abnormal liver function
	Bilirubin (hyperbilirubinemia) T bili >1.5 x ULN	docetaxel	Hold all treatment and re-evaluate within 7 days If recovered to <ULN, ↓ 1 dose level docetaxel If not recovered within 21 days, discontinue docetaxel
	ALT, SGPT (serum glutamic pyruvic transaminase) Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4
	Grade 3 or 4		Discontinue lapatinib permanently
	AST, SGOT (serum glutamic oxaloacetic transaminase) Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4
	Grade 3 or 4		Discontinue lapatinib permanently
Bilirubin (hyperbilirubinemia) Grade 2	lapatinib	See Section 8.5 Management of Abnormal Liver Function Tests and notes under Section 8.4	
Grade 3 or 4		Discontinue lapatinib permanently	
Neurology	Neuropathy, motor Grade 1 or 2	carboplatin docetaxel	Hold all treatment (maximum 21 days) until ≤Grade 1, then ↓ 1 dose level and re-treat
	Grade 3 or 4		Discontinue treatment
	Neuropathy, sensory Grade 1 or 2	carboplatin docetaxel	Hold all treatment (maximum 21 days) until ≤Grade 1, then ↓ 1 dose level and retreat
	Grade 3 or 4		Discontinue treatment
Other non-hematologic adverse events	≥Grade 3	carboplatin docetaxel lapatinib trastuzumab	Hold or omit treatment until the adverse event resolves to ≤Grade 1 then reinstate (if medically appropriate) at ↓ 1 dose level
	Grade 4		Permanently discontinue appropriate study drug(s)

10.0 Adverse Event (AE) Reporting and Monitoring

- Add 4
- 10.1 CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 will be utilized until March 31, 2010. CTCAE version 4.0 will be utilized for expedited adverse event reporting only, beginning April 1, 2011. All appropriate treatment areas should have access to a copy of the CTCAE v4.0. A copy of the CTCAE version 4.0 can be downloaded from the CTEP web site (<http://ctep.cancer.gov>).
- 10.11 Adverse event monitoring and reporting is a routine part of every clinical trial. First, identify and grade the severity of the event using the CTCAE. Next, determine whether the event is expected or unexpected (refer to Section 10.12) and if the adverse event is related to the medical treatment or procedure (see Section 10.13). With this information, determine whether an adverse event should be reported as an expedited report (see Section 10.2). **Important:** All AEs reported via expedited mechanisms must also be reported via the routine data reporting mechanisms defined by the protocol (see Section 10.3 and 18.0). Expedited adverse event reporting requires submission of an Adverse Event Expedited Reporting System (AdEERS) report(s). Other expedited reporting requirements and systems may also apply. Expedited and/or routine reports are to be completed within the timeframes and via the mechanisms specified in Sections 10.2 and 10.3. All expedited AE reports must also be sent to the local Institutional Review Board (IRB) according to local IRB's policies and procedures.
- Add 4
- Effective with Addendum 4, and beginning April 1, 2011, expedited AdEERS reporting for this protocol has been updated by the NCI/CTEP to use CTCAE v4.0. Therefore;
- 1) Events requiring expedited reporting through AdEERS must be reported through the AdEERS system in CTCAE v4.0.
 - 2) The events reported via AdEERS must ALSO be reported through routine reporting (i.e., Case Report Forms) using CTCAE v3.0.
 - 3) Routine data collection via Case Report Forms, including the "Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form," will remain using CTCAE v3.0 for this study.
- 10.12 Expected vs. Unexpected
- The determination of whether an AE is expected is based on the agent-specific information provided in Section 15.0 of this protocol.
 - Unexpected AEs are those not listed in the agent-specific information provided in Section 15.0 of this protocol.
- 10.13 Assessment of Attribution
- When assessing whether an adverse event is related to a medical treatment or procedure, the following attribution categories are utilized:
- Definite - The adverse event *is clearly related* to the agent(s).
- Probable - The adverse event *is likely related* to the agent(s).
- Possible - The adverse event *may be related* to the agent(s).
- Unlikely - The adverse event *is doubtfully related* to the agent(s).
- Unrelated - The adverse event *is clearly NOT related* to the agent(s).
- 10.14 Additional instructions for trials that include both investigational agent(s) (those under an IND) and a commercial agent(s):
- When an investigational agent (an agent under an IND) is used in combination with a commercial agent(s) on the same treatment arm, the combination is considered investigational. Expedited reporting will follow the requirements for investigational agents. However, if the event occurs prior to the participant having received any investigational agent, expedited reporting may follow the requirements for commercial agents.

10.2 Expedited Adverse Event Reporting Requirements

10.21 Requirements for Expedited **Investigational** Reporting via AdEERS for Adverse Events That Occur Within 30 Days¹ of the Last Dose of the Investigational Agent

	Grade 1	Grade 2	Grade 3		Grade 3		Grades 4 & 5
	Unexpected and Expected	Unexpected and Expected	Unexpected with Hospitalization	without Hospitalization	Expected with Hospitalization	without Hospitalization	Unexpected and Expected
Unrelated Unlikely	Not Required	Not Required	Not Required ²	Not Required	Not Required ²	Not Required	Not Required ²
Possible Probable Definite	Not Required	Not Required	7 Calendar Days	Not Required	7 Calendar Days	Not Required	24-Hour; 3 Calendar Days
<p>¹ Adverse events with attribution of possible, probable, or definite that occur <u>greater</u> than 30 days after the last dose of treatment with an agent under an IND require reporting as follows: AdEERS 24-hour notification followed by complete report within 3 calendar days for:</p> <ul style="list-style-type: none"> • Grade 3 unexpected events with hospitalization or prolongation of hospitalization • Grade 4 unexpected events • Grade 5 expected events and unexpected events <p>² Although expedited reporting via AdEERS is not required for hospitalizations or Grade 4 or 5 events with attribution of unlikely or unrelated, other expedited <u>and</u> routine reporting requirements must be adhered to. Please refer to the sections below for related instructions.</p> <p>Please see additional instructions and/or exceptions below under section entitled “Additional Instructions or Exceptions.”</p>							

- Expedited AE reporting timelines defined:
 - “24 hours; 3 calendar days” – The investigator must initially report the AE via AdEERS within 24 hours of learning of the event followed by a complete AdEERS report within 3 calendar days of the initial 24-hour report.
 - “7 calendar days” - A complete AdEERS report on the AE must be submitted within 7 calendar days of the investigator learning of the event.
- Any event that results in persistent or significant disability/incapacity, congenital anomaly, or birth defect must be reported via AdEERS if the event occurs following treatment with an agent under an IND.
- SECONDARY MALIGNANCIES (defined as “cancer caused by treatment for a previous malignancy,” e.g., treatment with radiation or chemotherapy) are to be reported through AdEERS, as noted in Section 10.22. Secondary malignancies are not considered metastasis of the initial neoplasm. Secondary malignancy is unrelated to the first cancer that was treated, and may occur months or even years after initial treatment.

Note: Second Primary malignancy (malignancy not due to prior treatment) should not be reported through AdEERS.

- Use the NCI protocol number and the protocol-specific patient ID provided during trial registration on all expedited reports.

Additional Instructions or Exceptions to AdEERS Expedited Reporting Requirements

- The NCCTG SAE Coordinator will forward a copy of all AdEERS reports to:
 - The NCCTG IND Coordinator who will notify the FDA as warranted by the event and stipulated in the U.S. Code of Federal Regulations.
 - GlaxoSmithKline Global Clinical Safety Program(GCSP) (*email address: us.naps@gsk.com or fax: 919-483-5404*)
- In the rare event when Internet connectivity is disrupted, a 24-hour notification is to be made to NCI by telephone at: 301-897-7497. An electronic report **MUST** be submitted immediately upon re-establishment of internet connection. Please note that all paper AdEERS forms have been removed from the CTEP web site and will **NO LONGER** be accepted.

Add 4

10.22 Other Required Expedited Reporting

Event Type	REPORTING PROCEDURE
Secondary AML/MDS	<p>Reporting for this event required during and after completion of study treatment via AdEERS.</p> <p>Through March 31, 2011, continue using CTCAE v3.0: Report Myelodysplasia as “Blood/Bone Marrow – Myelodysplasia” and Leukemias as “Blood/Bone Marrow – Other (Specify, _____).”</p> <p>Beginning April 1, 2011, AdEERS will only accept CTCAE v4.0 for this study. Report these events using “Neoplasms benign, malignant and unspecified (incl. cysts and polyps)” and including the appropriate adverse event:</p> <ul style="list-style-type: none"> - Leukemia secondary to oncology chemotherapy OR - Myelodysplastic syndrome OR - Treatment related secondary malignancy
Other Grade 4 or 5 Events and/or Any Hospitalizations During Treatment Not Otherwise Warranting an Expedited Report	<p>Complete a Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form within 5 working days, using CTCAE v3.0 of the date the clinical research associate (CRA) is aware of the event(s) necessitating the form.</p> <p>If an AdEERS report has been submitted, this form does not need to be submitted.</p> <p>You must use CTCAE v3.0 for data submission with this form. The events reported on this form must also appear on the Case Report Forms (i.e., routine data) for this study.</p> <p>Submit the Non-AER form electronically via the NCCTG Remote Data Entry System within 5 working days of the date the CRA is aware of the event(s) necessitating the form.</p> <p>The NCCTG SAE Coordinator will notify the NCCTG IND Coordinator who will submit to the FDA IND as warranted by the event and stipulated in the U.S. Code of Federal Regulations.</p>

Add 4

Add 4

- 10.3 Adverse events to be graded at each evaluation and pretreatment symptoms/conditions to be evaluated at baseline per Common Terminology Criteria for Adverse Events (CTCAE) v3.0 grading unless otherwise stated:

Add 4

Category (CTCAE v3.0)	Adverse Event/Symptoms	Baseline	Each evaluation
Allergy/Immunology	Allergic reaction/ hypersensitivity		X
Cardiac General	Left ventricular diastolic dysfunction	X	X
	Left ventricular systolic dysfunction	X	X
Constitutional Symptoms	Fatigue (lethargy, malaise, asthenia)	X	X
Dermatology/Skin	Rash/desquamation		X
Gastrointestinal	<i># of stools at baseline</i>	X	
	Diarrhea		X
	Mucositis/stomatitis (clinical exam) - Oral cavity - Pharynx		X
	Mucositis/stomatitis (functional/symptomatic) - Oral cavity - Pharynx		X
	Nausea		X
	Vomiting		X
Metabolic/ Laboratory	Alkaline phosphatase	X	X
	ALT, SGPT (serum glutamic pyruvic transaminase)	X	X
	ALT, SGOT (serum glutamic oxaloacetic transaminase)	X	X
	Bilirubin (hyperbilirubinemia)	X	X
Neurology	Neuropathy, motor		X
	Neuropathy, sensory		X
Pain	Pain - Bone	X	X
	Pain - Muscle	X	X
Pulmonary/Upper Respiratory	Cough	X	X
	Dyspnea	X	X

Add 4

- 10.31 Submit to the NCCTG Research Base via the Nadir/AE Log the following AEs using CTCAE v3.0 experienced by a patient and not specified in Section 10.3:
 - 10.311 Grade 2 AEs deemed *possibly, probably, or definitely* related to the study treatment or procedure.
 - 10.312 Grade 3 and 4 AEs regardless of attribution to the study treatment or procedure
 - 10.313 Grade 5 AEs (Deaths)
 - 10.3131 Any death within 30 days of the patient's last study treatment or procedure regardless of attribution to the study treatment or procedure
 - 10.3132 Any death more than 30 days after the patient's last study treatment or procedure that is felt to be at least possibly treatment related must also be submitted as a Grade 5 AE, with a CTCAE type and attribution assigned.
- 10.32 Refer to the instructions in the Forms Packet (or electronic data entry screens, as applicable) regarding the submission of late occurring AEs following completion of the Active Monitoring Phase (i.e., compliance with Test Schedule in Section 4.0).

18.0 Records and Data Collection Procedures

18.1 Submission Timetable

Forms	Active-Monitoring Phase (Compliance with Test Schedule)				Event-Monitoring Phase	At Each Occurrence				
	Pathology Quality Assurance Review	Initial Material	Follow-up material							
	≤30 days after registration	≤2 weeks after registration	At each evaluation	At end of treatment	q 3 mos for 1 yr, then q 6 mos for 2 nd year, then yearly for a max of 10 yrs from registration	At time of each breast cancer recurrence	ADR/AER	New Primary	Grade 4 or 5 Non-AER Reportable Events/Hospitalization	Late Adverse Event
On-Study Form		1								
Baseline Adverse Events Form		1								
Pathology Materials (See Section 17.0)	7									
OP and Path Reports	7	2								
Blood Specimen Submission Form (Section 14.0)		1,3	3							
Tissue Specimen Submission Form (Section 17.0)	7									
Concurrent Treatment Form(s)		1	1	X						
Adjuvant Breast Cancer Radiotherapy Report Form				4						
MUGA/Echo Reporting Form		1,5	5		5					
Congestive Heart Failure Report Form			1		X					
Cardiac Death Report Form			1	X	X					
Event Monitoring Form					X	X		X		X
Evaluation/Treatment Form Cycles 1-6			1	X						
Evaluation/Treatment Form Cycles 7-18			X	X						
Nadir/Adverse Event Form			1	X						
End of Active Treatment/ Cancel Notification Form		6		X						
ADR/AER (See Section 10.0)							X			
Grade 4 or 5 Non-AER Reportable Events/ Hospitalization Form									X	

Add 4

1. If one of first 10 patients registered, all expected CRFs (Baseline and Cycle 1) must be entered ≤14 days after completion of Cycle 1 (ie ≤14 days after Cycle 2, Day 1).
2. Submit second copy to the **NCCTG Operations Office**, Attention: QCS for N083E. (First copy is submitted with pathology materials.)
3. Blood specimens will be submitted at the following timepoints: Baseline (prior to tx on Cycle 1), after Cycle 6 Tx but prior to tx on Cycle 7(Weeks 19-20) at end of treatment (~52 weeks) and at recurrence.
4. For patients who do not receive any radiation therapy, submit the RT reporting form with the reason radiation was not given. For patients who receive partial/complete radiation therapy, submit the RT reporting from ≤14 days after the last day of radiation therapy.
5. LVEF assessment to be done Baseline, Cycle 6 ≥Day 15, Cycle 12, and Cycle 18. After 1 year, LVEF assessment is recommended annually, but can be done according to local standard of care
6. Submit if withdrawal/refusal prior to beginning protocol therapy occurs.
7. Mandatory pathology QA –submission of diagnostic materials to confirm diagnosis of HER2 positive breast cancer must be completed ≤30 days after registration (see Section 17.51).

N083E FORMS PACKET

N083E, Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in Early Breast Cancer

- Contents:
- Eligibility checklist (9/25/09)
 - * Forms completion instructions (9/10/04)
 - On-study form (12/17/08)
 - Pathology reporting form (2/16/09)
 - Pathology specimen submission form (2/18/09)
 - ✓ Baseline adverse events form (12/2/10)
 - ✓ Nadir/adverse event form (12/2/10)
 - Blood specimen submission form (5/6/10)
 - Baseline tissue specimen submission form (12/17/08)
 - Baseline concurrent treatment form (2/16/09)
 - Active monitoring concurrent treatment form (2/16/09)
 - Cycles 1-6 evaluation treatment form (2/16/09)
 - Cycles 7-18 evaluation treatment form (2/16/09)
 - Muga/echo reporting form (2/18/09)
 - Cardiac death report form (2/16/09)
 - Congestive heart failure report form (2/16/09)
 - Adjuvant breast cancer radiotherapy report form (12/17/08)
 - End of active treatment/cancel notification form (12/17/08)
 - Event monitoring form (12/17/08)
 - Grade 4 or 5 non-AER reportable events/hospitalization form (12/17/08)
 - Kit Supply Order Form

✓ designates revised/new forms

*Generic forms completion instructions are available on the NCCTG web site under “the CRA link in the Remote Registration and Data Entry section and are titled “Remote Data Entry Screen Instructions (Forms Completion)”

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N083E

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

**BASELINE
ADVERSE EVENTS FORM**

ALL ITEMS MUST BE COMPLETED

Are data amended? (*check one*) Yes No
(if data are amended, please circle in red when using paper form)

Required Baseline Adverse Events from Section 10.0 of Protocol		
CTC Adverse Event Term (CTCAE v3.0)	MedDRA Code (v. 10.0)	CTC Adverse Event Grade
Baseline number of stools per day: _____		
Left ventricular diastolic dysfunction	10049694	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Left ventricular systolic dysfunction	10024119	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Fatigue (asthenia, lethargy, malaise)	10016256	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Alkaline phosphatase	10001675	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
ALT, SGPT (serum glutamic pyruvic transaminase)	10001551	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
AST, SGOT (serum glutamic oxaloacetic transaminase)	10003481	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Bilirubin (hyperbilirubinemia)	10004690	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
<i>Pain - Selects</i>		
- Bone	10006002	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
- Muscle	10028411	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Cough	10011224	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3
Dyspnea (shortness of breath)	10013963	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N083E

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

NADIR/ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 1 of 4

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Current Cycle Number (nadir/adverse events associated with this cycle): _____

Date of evaluation: (mm/dd/yyyy) ____/____/____

Test	Nadir/Worst Date (Date of lab test) (mm/dd/yyyy)	Nadir/Worst Value (The nadir is the lowest value of counts occurring between two treatments. If the only count available is taken the day of retreatment, use that value as the nadir.)	Is nadir below LLN? (check one)	CTC AE Attribution Code (If Grade >0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?*(Enter 1 for Yes or 2 for No)
Platelets (PLT) K/uL or 10 ⁹ /L	____/____/____	____.	1 <input type="checkbox"/> Yes → 2 <input type="checkbox"/> No (Go to Hgb)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____
Hemoglobin (Hgb) g/dL	____/____/____	____.	1 <input type="checkbox"/> Yes → 2 <input type="checkbox"/> No → (Go to ANC)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____
Absolute Neutrophil Count (ANC) K/uL or 10 ⁹ /L	____/____/____	____.	1 <input type="checkbox"/> Yes → 2 <input type="checkbox"/> No → (Go to Adverse Event)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____

CTC Adverse Event Term (CTCAE v3.0)	MedDRA Code (v. 10.0) (must be completed)	CTC Adverse Event Grade (highest grade this cycle) INCLUDE GRADE 0's	CTC AE Attribution Code (If Grade > 0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?*(Enter 1 for Yes or 2 for No)
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Required Adverse Events from Section 10.0 of Protocol

Allergic reaction/hypersensitivity (including drug fever)	10020751	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____
Left ventricular diastolic dysfunction	10049694	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____
Left ventricular systolic dysfunction	10024119	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____
Fatigue (asthenia, lethargy, malaise)	10016256	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	____

* See Section 10.0 of the protocol.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

NADIR/ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 2 of 4

Are data amended? (check one) Yes No

(if data are amended, please circle in red when using paper form)

Protocol Number: N083E

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

Current Cycle Number (nadir/adverse events associated with this cycle): _____

CTC Adverse Event Term (CTCAE v3.0)	MedDRA Code (v. 10.0) (must be completed)	CTC Adverse Event Grade (highest grade this cycle) INCLUDE GRADE 0's	CTC AE Attribution Code (If Grade > 0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?*(Enter 1 for Yes or 2 for No)
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Required Adverse Events from Section 10.0 of Protocol

Rash/desquamation	10037853	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Diarrhea	10012727	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Mucositis/stomatitis (clinical exam) - <i>Selects</i>				
- Oral Cavity	10056848	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
- Pharynx	10065717	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Mucositis/stomatitis (functional/symptomatic) - <i>Selects</i>				
- Oral Cavity	10028130	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
- Pharynx	10065881	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Nausea	10028813	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Vomiting	10047700	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Alkaline phosphatase	10001675	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
ALT, SGPT (serum glutamic pyruvic transaminase)	10001551	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
AST, SGOT (serum glutamic oxaloacetic transaminase)	10003481	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Bilirubin (hyperbilirubinemia)	10004690	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Neuropathy: motor	10034580	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___
Neuropathy: sensory	10034620	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	___

* See Section 10.0 of the protocol.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N083E

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 3 of 4

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Current Cycle Number *(adverse events associated with this cycle)*: _____

CTC Adverse Event Term (CTCAE v3.0)	MedDRA Code (v. 10.0) <i>(must be completed)</i>	CTC Adverse Event Grade <i>(highest grade this cycle)</i> INCLUDE GRADE 0's	CTC AE Attribution Code (If Grade > 0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?* <i>(Enter 1 for Yes or 2 for No)</i>
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Required Adverse Events from Section 10.0 of Protocol

Pain - *Selects*

- Bone	10006002	0 1 2 3 4	1 2 3 4 5	_____
- Muscle	10028411	0 1 2 3 4	1 2 3 4 5	_____
Cough	10011224	0 1 2 3	1 2 3 4 5	_____
Dyspnea (shortness of breath)	10013963	0 1 2 3 4 5 (death)	1 2 3 4 5	_____

* See Section 10.0 of the protocol.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

NADIR/ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 4 of 4

Protocol Number: N083E

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Current Cycle Number (adverse events associated with this cycle): _____

Were (other) adverse events assessed during this report period?

1 Yes, and reportable adverse events occurred

3 Yes, but no reportable adverse events occurred (Stop here)

2 No (Stop here)



Adverse Events beyond those required in Section 10.0 of the protocol. Record grade 2 with attribution of possible, probable or definite and all grade 3, 4 and 5 regardless of attribution.**

Other CTC Adverse Event Term not listed (CTCAE v3.0)	MedDRA Code (v. 10.0) (must be completed)	CTC Adverse Event Grade (highest grade this cycle)	CTC AE Attribution Code (If Grade > 0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?*(Enter 1 for Yes or 2 for No)
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 (death)	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	—

* See Section 10.0 of the protocol.

** Both hematologic (except for the nadirs listed on page 1) and nonhematologic Adverse Events must be graded on this form as applicable.