

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 15 – November 26, 2010

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 7.21, 8.0, 10.21, 10.22, 10.23, 10.3, 10.31, and 16.327). Effective January 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.

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

Title Page Updated to reflect Addendum 15 and revised NCI version date.

Section 7.0 **Protocol Treatment**
Page 19: Due to the CTCAE conversion, the heading of the first column in Section 7.21 has been updated for clarification as follows:
Toxicity (CTCAE v3.0)

Section 8.0 **Dosage Modification Based on Adverse Events**
Page 26: The first column header in the Section 8.0 table has been revised for clarification as follows:

CTCAE V3.0 CATEGORY

Section 10.0 Adverse Event (AE) Reporting and Monitoring

Pages 27-28:

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.

- 10.1 ~~This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 for adverse event 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 December 31, 2010 for AE reporting. CTCAE v4.0 will be utilized for expedited adverse event reporting only, beginning January 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 ...

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

Effective with Addendum 14, and beginning January 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.**

Pages 29/31:

The second bullet under Sections 10.21 and 10.22 tables have been revised for clarification as follows:

Any medical event equivalent to CTCAE **v4.0** grade 3, 4, or 5...

Text has been added at the bottom of the table (right hand column) in Section 10.23 for clarification, as follows:

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.

Page 30:

The first sentence in the first bullet under "Additional Instructions or Exceptions..." in Section 10.21 has been corrected as follows:

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, ~~or 301-897-7402 for CIP studies.~~

- Page 31: The first bullet under the “Additional Instructions...” section in Section 10.22 has been revised to reflect updated notification instructions 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>). Refer to CTEP, NCI Guidelines: Adverse Event Reporting Requirements for back up submission instructions. When internet connectivity is interrupted, a 24-hour notification is made to CTEP by telephone at 301-897-7497. Once internet connectivity is restored, an AE report submitted on a paper template or a 24-hour notification that is called in, must be entered into electronic AdEERS by the original submitter of the report at the site.~~ **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 website and will NO LONGER be accepted.**
- Pages 32-33: Section 10.3 and Section 10.31 have been revised for clarification. In Section 10.3 the first column header in the chart has added **v3.0** and Section 10.31 has been revised as follows:
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...
- Section 16.0** **Statistical Considerations and Methodology**
- Page 49: The last sentence in Section 16.327 has been added for clarification as follows:
CTCAE v3.0 will be used to determine grading for these stopping rules.

North Central Cancer Treatment Group

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

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

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DCTD Supplied Investigational Agents: PS-341 (NSC #681239)

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

√Study contributor not responsible for patient care.

Document History	(Effective Date)	Document History	(Effective Date)
Activation	September 17, 2004	Addendum 8	January 18, 2008
Addendum 1	February 11, 2005	Addendum 9	June 13, 2008
Update 1	February 11, 2005	Addendum 10	August 29, 2008
Addendum 2	July 29, 2005	Addendum 11	February 20, 2009
Addendum 3	March 17, 2006	Addendum 12	October 9, 2009
Addendum 4	August 18, 2006	Addendum 13	April 16, 2010
Addendum 5	February 2, 2007	Addendum 14	November 5, 2010
Addendum 6	June 8, 2007	Addendum 15	November 26, 2010
Addendum 7	June 8, 2007		

Study Participants **Date Activated**
Entire NCCTG September 17, 2004
NCI Version Date: November 9, 2010

7.13 Dose Escalation

Dose level	PS-341 mg/m ²	Paclitaxel mg/m ²	CBDCA AUC
-1	0.5	120	5
0	0.5	135	5
*1	0.5	150	5
2	0.8	150	5
3	1.0	150	5
4	1.0	175	5
5	1.0	175	6
6	1.2	175	6

Add 9

***starting dose level**

7.14 Treatment by a local medical doctor is not allowed.

7.15 Three patients will be treated at each dose level and observed for a minimum of 4 weeks, to assess toxicities, before new patients are treated. Doses will not be escalated in any individual patient.

7.16 Dose escalation from one level to the next cannot occur until all patients enrolled on a specific dose level have completed RT.

Add 1

7.17 Investigators are to contact the NCCTG Operations Office (507-538-1079) as soon as any dose-limiting toxicity occurs.

7.2 Definitions of DLT

7.21 For this protocol, dose-limiting toxicity (DLT) will be defined as follows:

Add 15

Toxicity (CTCAE v3.0*)

Definition

Add 3

Skin

Grade ≥4 radiation dermatitis

Hematologic (ANC, PLT)**

Grade ≥4 for ≥8 days

Grade ≥4 febrile neutropenia

(ANC <1000/mm³ & fever ≥38.5°C)

PLT <25,000/ mm³

Esophagitis

Grade ≥3 requiring hospitalization

Pneumonitis

Grade ≥3 (requiring O₂)

Dyspnea

Grade ≥4 (at rest)

Other non-hematologic

Grade ≥4 that is not manageable with medical interventions (IV, narcotic) as per NCI Common Terminology Criteria for Adverse Events (CTCAE) v3.0

Add 3

*Adverse event at least possibly related to the study medication.

**Cycle 1 of chemotherapy only.

7.22 MTD Determination

Aggressive radiotherapy and chemotherapy for lung cancer is associated with significant toxicity. In an analysis of 5 RTOG chemo/RT studies, the incidence of

8.0 Dosage Modification Based on Adverse Events – Strictly follow the modifications in this table for the first **two** cycles, until individual treatment tolerance can be ascertained. Thereafter, these modifications should be regarded as guidelines to produce mild-to-moderate, but not debilitating, side effects. If multiple adverse events are seen, administer dose based on greatest reduction required for any single adverse event observed. Reductions or increases apply to treatment given in the preceding cycle and are based on adverse events observed since the prior dose.

ALERT: ADR reporting may be required for some adverse events (See Section 10)

→→ Use Common Terminology Criteria for Adverse Events (CTCAE) v. 3.0 unless otherwise specified ←←

CTCAE V3.0 Category	Adverse Event	Agent(s)	Action
<i>Blood/Bone Marrow</i>	ANC ¹ <500 or PLT <20,000	RT PS-341 CBDCA TAXOL	Hold RT, PS-341, CBDCA and TAXOL until ANC ≥ 1000 and PLT ≥ 50,000 and fever absent and/or dysphagia ≤ grade 2. Resume treatment with PS-341, CBDCA and TAXOL doses reduced by 50%. If toxicity recurs, hold all treatment modalities as above. Resume treatment without PS-341, CBDCA and TAXOL ³ .
<i>Infection</i>	Febrile neutropenia ²		
<i>Gastrointestinal</i>	Dysphagia, grade 4		
	Dysphagia, grade 3		
	Nausea/vomiting grade 3 or 4, not controlled with optimal medication		
<i>Other non-hematologic</i>	Grade 3 or greater		
<i>Neurology</i>	Neuropathy: motor Grade 2	PS-341 CBDCA TAXOL	Decrease dose by 30%. If persists, continue to decrease by 30%.
	Neuropathy: sensory Grade 3 or 4		Discontinue PS-341, CBDCA and TAXOL, continue RT.

1. ANC - Absolute neutrophil count
2. Temperature ≥38.5°C with ANC <1000 or severe infection
3. If RT or chemotherapy is suspended for toxicity, patient evaluation should continue at least weekly and hematologic parameter should continue weekly. Patient should go off study if treatment is held for more than 2 weeks, except as clarified in item 4, below.
4. In a patient who is responding to therapy, this dose modification table should be viewed as guidelines. Adjustments can be made to chemotherapy doses in consultation with the PI, so that the patient can remain on study and derive full benefit from treatment.

Add 15

9.0 Ancillary Treatment

- 9.1 Patients should receive full supportive care while on this study. This includes blood-product support, antibiotic treatment, nutritional evaluation and treatment of other newly diagnosed or concurrent medical conditions. All blood products and concomitant medications such as anti-diarrheals, analgesics, antiemetics, and medications used for the prevention and treatment of radiation esophagitis from the beginning of treatment until 28 days after the final radiation therapy dose should be recorded in the medical records.
- 9.2 Anti-emetics: Anti-emetics should be prescribed by the treating physician as clinically indicated, if a patient develops nausea and/or vomiting. A suggested anti-emetic regimen is as follows: For severe nausea/and or vomiting, patients could receive granisetron 1mg po pretreatment, together with dexamethasone 20 mg po followed by granisetron 1 mg po BID x 24 hours with dexamethasone 4 mg bid x 48 hours. Prochlorperazine 10 mg po every six hours as needed and lorazepam 1 mg every 4 hours as needed may be prescribed as well.
- 9.3 Diarrhea: A suggested anti-diarrheal regimen is as follows: Loperamide (Imodium®): 4 mg, followed by 2 mg every 2 hours until patients are free of diarrhea for at least 12 hours. At night, 4 mg of loperamide should be taken every 4 hours. Diphenoxylate/atropine (Lomotil™) (doses per physician discretion) may be substituted for loperamide.
- 9.4 Growth Factors: Routine use of a colony-stimulating factor (G-CSF or GM-CSF) is not recommended. Prophylactic use of colony stimulating factors during the study is not allowed. Therapeutic use in patients with serious neutropenic complications such as tissue infection, sepsis syndrome, fungal infection, etc. may be considered at the investigator's discretion. Recombinant erythropoietin to maintain adequate hemoglobin levels and avoid packed red blood cell transfusions is allowed.

10.0 Adverse Event (AE) Reporting and Monitoring

- Add 2,15 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 December 31, 2010 for AE reporting. CTCAE v4.0 will be utilized for expedited adverse event reporting only, beginning January 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>).
- Add 2 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 (see 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 the event must 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 Sections 10.3 and 18.0).
- Add 2 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 routine reports are to be completed within the timeframes and via the mechanisms specified in Section 10.2. All expedited AE reports must also be submitted to the local Institutional Review Board (IRB) according to local IRB's policies and procedures.

- Add 15 Effective with Addendum 15, and beginning January 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.
- Add 2 10.12 Expected vs. Unexpected Events
- Agent(s) under a CTEP IND:
- Add 3 • Expected AEs for expedited reporting purposes are listed on the CTEP Agent Specific Adverse Event List (ASAEL), a component of the Comprehensive Adverse Events and Potential Risks List (CAEPR). Refer to Section 15.0 to locate the CAEPR for the CTEP IND agent(s).
 - Unexpected AEs are those not listed in the ASAEL.
- Add 2 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).
- Add 2 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.

Add 2

10.21 Phase 1 Trials Utilizing an Agent under a CTEP IND: AdEERS Expedited Reporting Requirements for Adverse Events That Occur Within 30 Days¹ of the Last Dose of the Investigational Agent

	Grade 1	Grade 2	Grade 2	Grade 3		Grade 3		Grades 4 & 5 ²
	Unexpected and Expected	Unexpected	Expected	Unexpected with Hospitalization	without Hospitalization	Expected with Hospitalization	without Hospitalization	Unexpected and Expected
Unrelated Unlikely	Not Required	Not Required	Not Required	7 Calendar Days	Not Required	7 Calendar Days	Not Required	24-Hour; 3 Calendar Days
Possible Probable Definite	Not Required	7 Calendar Days	Not Required	24-Hour; 3 Calendar Days	24-Hour; 3 Calendar Days	7 Calendar Days	Not Required	24-Hour; 3 Calendar Days

¹ Adverse events with attribution of possible, probable, or definite that occur greater 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:

- Grade 3 unexpected events with hospitalization or prolongation of hospitalization
- Grade 4 unexpected events
- Grade 5 expected events and unexpected events

² Although an AdEERS 24-hour notification is not required for death clearly related to progressive disease, a full report is required as outlined in the table.

Please see additional instructions and/or exceptions below under section entitled "Additional Instructions or Exceptions."
 March 2005

Note: All deaths on study require both routine and expedited reporting regardless of causality. Attribution to treatment or other cause should be provided.

Add 15

Add 14

- 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 medical event equivalent to CTCAE v4.0 grade 3, 4, or 5 that precipitates hospitalization (or prolongation of existing hospitalization) must be reported regardless of attribution and designation as expected or unexpected with the exception of any events identified as protocol-specific expedited adverse event reporting exclusions.
- 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 a CTEP 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 10.23. 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 reports.

- 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 in the table below:

Add
15

CTCAE v3.0 Category	Adverse Event/symptoms	Baseline	Each evaluation
<i>Allergy/Immunology</i>	Allergic reaction/hypersensitivity (including drug fever)		X
<i>Constitutional Symptoms</i>	Fatigue (lethargy, malaise, asthenia)	X	X
	Fever (in the absence of neutropenia, where neutropenia is defined as AGC <1.0 x 10 ⁹ /L)		X
<i>Dermatology/Skin</i>	Rash: dermatitis associated with radiation -Chemoradiation		X
<i>Gastrointestinal</i>	# stools/day	X	
	Diarrhea		X
	Dysphagia (difficulty swallowing)	X	X
	Mucositis/stomatitis (clinical exam) -Oral Cavity or pharynx		X
	Mucositis/stomatitis (functional symptomatic) -Esophagus -Oral Cavity		X
	Nausea	X	X
	Vomiting	X	X
<i>Infection</i>	Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC < 1.0 x 10 ⁹ /L, fever ≥ 38.5°C)		X
<i>Neurology</i>	Neuropathy: motor	X	X
	Neuropathy: sensory	X	X
	Somnolence/depressed level of consciousness	X	X
<i>Pain</i>	Musculoskeletal -muscle	X	X
<i>Pulmonary/Upper Respiratory</i>	Dyspnea (shortness of breath)	X	X
	Pneumonitis/Pulmonary infiltrates	X	X

- Add 15 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 1 & 2 AEs deemed *possibly, probably, or definitely* related to the study treatment or procedure.
- Add 2 10.312 Grade 3 and 4 AEs regardless of attribution to the study treatment or procedure.
- Add 2 10.313 Grade 5 AEs (Deaths)
- Add 2 10.3131 Any death within 30 days after the patient's last treatment, regardless of relationship to study treatment or procedure.
- Add 2 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).

11.0 Treatment Evaluation Using RECIST Criteria²⁰

- Add 3 11.1 Schedule of Evaluations: Patients should ideally be reevaluated at 4 weeks post-RT, 3 months post-RT, every 3 months for 1 year post-RT, and every 6 months thereafter for a maximum of 5 years from time of registration (see below).
- 11.2 Definitions of Measurable and Non-Measurable Disease
- 11.21 Measurable disease is defined as at least one lesion whose longest diameter can be accurately measured as ≥ 2.0 cm with conventional techniques or as ≥ 1.0 cm with spiral CT. Clinical lesions will only be considered measurable when they are superficial (e.g., skin nodules, palpable lymph nodes). Lesions on chest x-ray are acceptable as measurable lesions when they are clearly defined and surrounded by aerated lung. However, CT is preferable.
- 11.22 All other lesions (or sites of disease), including small lesions (longest diameter < 2.0 cm with conventional techniques or as < 1.0 cm with spiral CT) are considered non-measurable disease. Bone lesions leptomeningeal disease, ascites, pleural/pericardial effusions, lymphangitis cutis/pulmonis, inflammatory breast disease, abdominal masses (not followed by CR or MRI), and cystic lesions are all non-measurable.
- 11.3 Guidelines for Evaluation of Measurable Disease
- 11.31 Measurement Methods:
- All measurements should be recorded in metric notation (i.e., decimal fractions of centimeters) using a ruler or calipers.
 - The same method of assessment and the same technique must be used to characterize each identified and reported lesion at baseline and during follow-up. For patients having only lesions measuring at least 1 cm to less than 2 cm must use spiral CT imaging for both pre- and post-treatment tumor assessments.
- Add 4

- After determining $\lambda = -\ln(.615)$, then $S(.5)$ was calculated using $S(t) = \exp(\ln(.615)*t)$.
- $S(.5)$ was found to equal .784 which led to a value of 20 of 26 patients alive at 6-months as a decision cutpoint for 6-month survival (being slightly conservative).

16.325 Stage 2: Enter an additional 40 patients (ie. 34 per study design + 6 over accrual) into the study. If 40 or fewer successes are observed in the first 60 evaluable patients, we will consider this regimen ineffective in this patient population and terminate the study. If 41 or more successes are observed in the first 60 evaluable patients, we will conclude that this treatment regimen has adequate evidence of efficacy and may be recommended for further testing in subsequent studies.

16.326 Over Accrual: If more than the target number of patients are accrued, the additional patients will not be used to evaluate the stopping rule at the interim analyses or the final decision rule. However, they will be included in the final analyses, which is described in section 16.35.

16.327 Toxicity Stopping Rule for Phase II portion: Based on our experience with previous regimens (i.e., 942452, 982452, 982453, N0026) in this patient population, we expect approximately 20% of patients to experience Grade 4 or 5 toxicities (treatment related AEs). If at any time, 7 of the initial 20 patients or 35% of all patients (i.e., when accrual is greater than 20 patients), have experienced any Grade 4+ non-hematologic toxicities or Grade 4+ thrombocytopenia, or, Grade 4+ complications from neutropenia (fever or infection), accrual to the study will be suspended to allow for a full review of the data. After consideration by the study team [ie, Study Chair(s), Statistician, Operations Office, etc] and consultation with representatives at the primary Internal Review Board (IRB) affiliated with the Operations Office, a decision will be made as to whether and how the study will proceed. CTCAE v3.0 will be used to determine grading for these stopping rules.

Add 15

16.33 Power and Significance Level: The probability values shown in the table below were calculated by using the following simulation: A sample of size 60 survival times were randomly selected 20,000 times from an exponential survival model ($S(t) = \exp(-\lambda t)$), where $\lambda = -\ln(\text{true success proportion})$ and $t = \text{time}$. Based on the sampled survival times and the 6-month interim analysis cutpoint determined in section 16.324; the power and the probability of stopping at the interim analysis (using just the first 26 patients from each trial) were calculated. The simulation resulted in a significance level of .09 and a power of .81 (assuming the true success proportion was .75).