Summary of Changes Page
BMT CTN 0702 STaMINA
Version 8.0 January 25, 2016

The following changes, and the rationale for the changes, were made to the attached protocol in this amendment.

Section number and title in Amendment 7.0	Section number and title in Amendment 8.0	Original text:	Changed to:	Rationale
Cover Page	Cover Page	Version 7.0	Version 8.0	Updated version number to indicate changes made since last DSMB review
Footnote	Footnote	Version 7.0 dated September 29, 2014	Version 8.0 dated January 25, 2016	Updated Version number and date to indicate changes made since last DSMB review
2.2.2 Study Objectives	2.2.2 Study Objectives	Comparing Grade ≥ 3 toxicities, graded according to the Common Terminology Criteria for Adverse Events (CTCAE), that occur within time periods that end approximately after each autologous transplantation, consolidation and yearly until 3 years post-randomization or until disease progression	Comparing Grade ≥ 3 toxicities, graded according to the Common Terminology Criteria for Adverse Events (CTCAE version 3.0), that occur within time periods that end approximately after each autologous transplantation, consolidation and yearly until 3 years post-randomization or until disease progression	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities
2.3.2 Initial Patient Exclusion Criteria	2.3.2 Initial Patient Exclusion Criteria	Patients with >grade 2 sensory neuropathy (CTCAE).	Patients with >grade 2 sensory neuropathy (CTCAE version 3.0).	Updated language to clarify that CTCAE version 3.0 should be

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				used for grading toxicities
2.6.2 Therapy Toxicities	2.6.2 Therapy Toxicities	All toxicities will be graded using the Common Terminology Criteria for Adverse Events (CTCAE) with BMT specific definitions when appropriate.	All toxicities will be graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 with BMT specific definitions when appropriate.	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities
3.5.4 Incidence of Toxicities > 3 per CTCAE	3.5.4 Incidence of Toxicities > 3 per CTCAE Version 3.0	3.5.4 Incidence of Toxicities > 3 per CTCAE	3.5.4 Incidence of Toxicities > 3 per CTCAE Version 3.0	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities
4.2.3 Adverse Event Reporting	4.2.3 Adverse Event Reporting	Adverse events will be reported according to procedures specified in the BMT CTN MOP. Unexpected, grade 3-5 adverse events (AE) will be reported through an expedited AE reporting system.	Adverse events will be reported according to procedures specified in the BMT CTN MOP. Unexpected, grade 3-5 adverse events (AE) will be reported through an expedited AE reporting system using NCI's Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.	Updated language to clarify that CTCAE version 4.0 should be used for grading Adverse Events
4.2.3 Adverse Event Reporting	4.2.3 Adverse Event Reporting	Expected AEs will be reported using NCI's Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 at regular intervals as defined on the Form Submission Schedule.	Expected AEs will be reported using CTCAE version 3.0 at regular intervals as defined on the Form Submission Schedule.	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities

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4.2.3 Adverse Event Reporting	4.2.3 Adverse Event Reporting	All second primary malignancies (SPM), excluding non-melanoma skin cancers, experienced by patients enrolled on the study will be reported using the Unexpected, Grades 3-5 Adverse Event forms (AE1-AE6) in AdvantageEDC and must be reported within three business days of knowledge of the event. The Event Description of the Unexpected, Grades 3-5 Adverse Event forms should include histologic type.	All second primary malignancies (SPM), excluding non-melanoma skin cancers, experienced by patients enrolled on the study will be reported using the Adverse Event forms (AE1-AE6) in AdvantageEDC and must be reported within three business days of knowledge of the event. The Event Description of the Adverse Event forms should include histologic type.	Updated language to be consistent with name of eCRF that collects Adverse Event Data.
4.2.3 Adverse Event Reporting	4.2.3 Adverse Event Reporting	The descriptions and grading scales found in the CTEP version 3.0 of the NCI Common Terminology Criteria for Adverse Events (CTCAE) will be utilized for AE reporting. The CTEP version 3.0 of the CTCAE is identified and located on the CTEP website at (http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm). All appropriate treatment areas should have access to a copy of the CTEP version 3.0 of the CTCAE.	The descriptions and grading scales found in the CTEP version 4.0 of the NCI Common Terminology Criteria for Adverse Events (CTCAE) will be utilized for AE reporting. The CTEP version 4.0 of the CTCAE is identified and located on the CTEP website at (http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm). All appropriate treatment areas should have access to a copy of the CTEP version 3.0 (for toxicity) and 4.0(for AE reporting) of the CTCAE.	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities and version 4.0 should be used for grading adverse events

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N/A	4.2.3.1 Adverse Event Reporting Following Progression	N/A	If a patient meets the protocol defined definition of progression (Chapter 3), Unexpected Grade 3-5 Adverse Events and events listed in Appendix K areno longer required to be reported on the Adverse Event Form once the patient is more than 28 days from their last dose of lenalidomide. However, SPMs should continue to be reported within three business days of the knowledge of the event through the end of the study follow up period.	Updated language to clarify how adverse events should be reported following progression. See intro memo for further justification of this change.
N/A	4.2.3.2 Adverse Event Reporting Following an SPM	N/A	Adverse Event reporting following an SPM is dependent on the treatment received for the reported SPM. - If a patient experiences an SPM resulting in permanent discontinuation of lenalidomide and initiation of non-protocol systemic therapy, Unexpected Grade 3-5 Adverse Events and events listed in Appendix K will are no longer required to be reported on the Adverse Event Form once the patient is more than 28 days from their last dose of lenalidomide.	Updated language to clarify how adverse events should be reported following occurrence of an SPM. See intro memo for further justification of this change.

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			- If a patient experiences an SPM that does *not* result in permanent discontinuation of lenalidomide, Adverse Events will continue to be reported as per section 4.2.3 and appendix K of the protocol. - Requests to discontinue Adverse Event Reporting for events that do not meet the criteria above will be considered on a case by case basis.	
Section 4.2.4.5 Laboratory Disease Response Assessment	Section 4.2.4.5 Laboratory Disease Response Assessmen	1. Laboratory Disease Response Assessments a. Quantitative serum immunoglobulin levels. b. Serum protein electrophoresis (SPEP). c. 24 hour urine collection to determine creatinine clearance and protein excretion, urine protein electrophoresis (UPEP). d. Immunofixation electrophoresis of serum protein and urine protein regardless of SPEP and UPEP results. e. Serum beta 2 microglobulin	2. Laboratory Disease Response Assessments a. Quantitative serum immunoglobulin levels. b. Serum protein electrophoresis (SPEP). c. 24 hour urine collection to determine urine protein electrophoresis (UPEP). d. Immunofixation electrophoresis of serum protein and urine protein regardless of SPEP and UPEP results. e. Serum free light chain ratio (FLC ratio).	Updated language to remove requirement for creatinine clearance and Serum Beta 2 Microglobulin as part of a disease response assessment. These were included in previous versions in error

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		(B2M Serum) f. Serum free light chain ratio (FLC ratio).		
Section 5.10 Analysis of the Secondary Endpoints	Section 5.10 Analysis of the Secondary Endpoints	The incidence of toxicities of grade 3 or higher toxicities (CTCAE), the incidence of probable viral fungal and bacterial infections, and the incidence of treatment-related morality	The incidence of toxicities of grade 3 or higher toxicities (CTCAE version 3.0), the incidence of probable viral fungal and bacterial infections, and the incidence of treatment-related morality	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities
Section 5.10 Analysis of the Secondary Endpoints	Section 5.10 Analysis of the Secondary Endpoints	**Incidence of Toxicities Grade ≥ 3 per CTCAE**	**Incidence of Toxicities Grade ≥ 3 per CTCAE Version 3.0**	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities
Appendix K-Adverse Events	Appendix K-Adverse Events	The calendar-driven forms are the Toxicity, Neurotoxicity Assessment Tool and Hem/Chem Forms. Event-driven forms include hospitalization, death, infection, thromboembolism forms and Individual Case Safety Report (ICSR). Selected expected serious AEs and grade 3-4 unexpected AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) require expediting reporting with an ICSR. Additionally for selected AEs collected	The calendar-driven forms are the Toxicity, Neurotoxicity Assessment Tool and Hem/Chem Forms. Event-driven forms include hospitalization, death, infection, thromboembolism forms and adverse event forms, also referred to as Individual Case Safety Report (ICSR). Selected expected serious AEs and grade 3-4 unexpected AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 require expediting reporting with an ICSR. Additionally for	Updated language to clarify that CTCAE version 3.0 should be used for grading toxicities and version 4.0 should be used for grading adverse events. Additionally, clarified where language regarding adverse event reporting can be found in the protocol.

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		in calendar-driven form (Table K-3) will require expedited reporting through an ICSR, if they fulfill criteria for serious AE and occur after the administration of bortezomib or lenalidomide.	selected AEs collected in calendar-driven form (Table K-3) will require expedited reporting through an ICSR, if they fulfill criteria for serious AE and occur after the administration of bortezomib or lenalidomide. Refer to Chapter 4 regarding reporting of SPMs and other reporting requirements.	