Summary of Changes Page
BMT CTN 1102 Protocol Amendment #4
Dated September 20, 2018

Section number and title in Version 4.0	Section number and title in Amendment	Original Text	Changed To	Rationale
Protocol Team	Protocol Team	**Protocol Team:** Joseph Alvarnas, MD[1] Frederick Appelbaum, MD[3] Adam Mendizabal, PhD[4] Richard Champlin, MD[5] Dennis Confer, MD[6] Steve Forman, MD[1] Steven D. Gore, MD[7] Mary Horowitz, MD, MS[8] Jennifer Le Rademacher, PhD[8] Eric Leifer, PhD[9] Moira Lewis, MPH[4] Brent Logan, PhD[8] Betul Oran, MD[5] Joycelynne Palmer, PhD[1] Marcelo Pasquini, MD[8] Alyssa Ramirez[4] Scott Ramsey, MD, PhD[3] Wael Saber, MD, MS[8] Bart Scott, MD[3] Mikkael Sekeres, MD, MS[10] Richard Stone, MD[2]	**Protocol Team:** Joseph Alvarnas, MD[1] Frederick Appelbaum, MD[3] Adam Mendizabal, PhD[4] Richard Champlin, MD[5] Dennis Confer, MD[6] Steve Forman, MD[1] Steven D. Gore, MD[7] Mary Horowitz, MD, MS[8] Eric Leifer, PhD[9] Brent Logan, PhD[8] Michael Martens, PhD[4] Betul Oran, MD[5] Joycelynne Palmer, PhD[1] Marcelo Pasquini, MD[8] Alyssa Ramirez[4] Scott Ramsey, MD, PhD[3] Wael Saber, MD, MS[8] Bart Scott, MD[3] Mikkael Sekeres, MD, MS[10] Richard Stone, MD[2]	Jennifer LeRademacher and Moira Lewis are no longer on the protocol team. Michael Martens is now on the protocol team.
Study Participants Page	(Page has been deleted)	**Core Study Participants** … **Affiliate Study Participants** …	--	We no longer include the page of study participants in protocol documents.

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Section 2.3.2 Patient Exclusion Criteria	Section 2.3.2 Patient Exclusion Criteria	Patients with the following will be ineligible for enrollment onto this study: 1. Therapy-related MDS (defined as the occurrence of MDS due to prior exposure to systemic chemotherapy and/or radiation for malignancy)	Patients with the following will be ineligible for enrollment onto this study: 1. Therapy-related MDS (defined as the occurrence of MDS due to prior exposure to systemic chemotherapy and/or radiation)	The words 'for malignancy' were removed because any prior exposure to systemic chemotherapy and/or radiation could lead to MDS, it does not matter what they were used for.
Section 4.4.2 Follow-up schedule for HCT Arm	Section 4.4.2 Follow-up schedule for HCT Arm	Patients in the HCT arm will be followed according to each HCT center's institutional standard.	Patients in the HCT arm will be followed according to each HCT center's institutional standard and data will be reported every 3 months for Year 1 and 2 (+/- 1 month) and every 6 months in Year 3 (+/- 2 months) in AdvantageEDC.	Clarification that HCT arm patients also have data reported regularly in AdvantageEDC.
Section 4.5 OPTIONAL Research Samples Pre-transplant and at Relapse (RIC alloHCT Arm only)	Section 4.5 OPTIONAL Research Samples Pre-transplant and at Relapse (RIC alloHCT Arm only)	In addition to research samples at enrollment (Section 4.1.2) collected from consenting patients, a pre-transplant bone marrow sample (1 mL) will be collected for those assigned to the alloHCT arm.	In addition to research samples at enrollment (Section 4.1.2) collected from consenting patients, a pre-transplant bone marrow sample (1 mL) will be collected for those assigned to the alloHCT arm (within 3 months prior to transplant).	The time frame in which the pre-transplant bone marrow sample should be collected was clarified.
Section 5.1.3. Intention-to-Treat Principle	Section 5.1.3. Intention-to-Treat Principle	Secondary analyses using as-treated principle will be considered.	Secondary analyses using an as-treated principle will be considered.	Grammatical correction.
Section 5.2 Sample Size and Power Calculations	Section 5.2 Sample Size and Power Calculations	The primary analysis will compare estimated three-year OS probabilities between arms using the Kaplan Meier estimator. Without censoring, the three-year OS probabilities reduce to simple binomial proportions. A point-wise comparison of survival at three years is	The primary analysis will compare three-year OS probabilities between arms using adjusted survival estimates provided by the method of Zhang et al[1] to account for potential differences in baseline covariates. Without censoring or covariates, the three-year OS probabilities reduce to simple	Clarification that the primary endpoint analysis will use covariate-adjusted survival probability estimates. Version 4.0 is inconsistent,

<table>
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<tr><td></td><td></td><td>proposed for the primary analysis rather than the log rank test because of the potential for crossing hazards. The log rank test would have lower power to detect a difference between two groups in case of crossing hazards. The sample size calculations were based on two-sample Z test of binomial proportions.</td><td>binomial proportions. A point-wise comparison of survival at three years is proposed for the primary analysis rather than the Cox proportional hazards model because of the potential for crossing hazards. The Cox model would have lower power to detect a difference between two groups in the presence of crossing hazards. The sample size calculations were based on a two-sample Z test of binomial proportions.</td><td>mentioning unadjusted Kaplan-Meier estimates here and adjusted estimates in Section 5.5.1.</td></tr>
<tr><td>TABLE 5.2 POWER TO DETECT 15% INCREASE IN OS PROBABILITY IN THE TRANSPLANT ARM FOR VARIOUS SURVIVAL PROBABILITIES AND PROPORTIONS OF DONOR AVAILABILITY</td><td>TABLE 5.2 POWER TO DETECT 15% INCREASE IN OS PROBABILITY IN THE TRANSPLANT ARM FOR VARIOUS SURVIVAL PROBABILITIES AND PROPORTIONS OF DONOR AVAILABILITY</td><td><table>
<tr><th rowspan="2">Donor Availability</th><th rowspan="2">Total Sample size (HCT, Non-HCT)</th><th colspan="2">Three-year OS</th><th rowspan="2">Power</th></tr>
<tr><th>HCT</th><th>Non-HCT</th></tr>
<tr><td rowspan="2">60%</td><td rowspan="2">338
(203, 135)</td><td>35%</td><td>20%</td><td>83%</td></tr>
<tr><td>40%</td><td>25%</td><td>80%</td></tr>
<tr><td rowspan="2">70%</td><td rowspan="2">400
(280, 120)</td><td>35%</td><td>20%</td><td>84%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
</table></td><td><table>
<tr><th rowspan="2">Donor Availability</th><th rowspan="2">Total Sample size (HCT, Non-HCT)</th><th colspan="2">Three-year OS</th><th rowspan="2">Power</th></tr>
<tr><th>HCT</th><th>Non-HCT</th></tr>
<tr><td rowspan="2">60%</td><td rowspan="2">338
(203, 135)</td><td>35%</td><td>20%</td><td>83%</td></tr>
<tr><td>40%</td><td>25%</td><td>80%</td></tr>
<tr><td rowspan="2">62%</td><td rowspan="2">343
(213, 130)</td><td>35%</td><td>20%</td><td>85%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
<tr><td rowspan="2">64%</td><td rowspan="2">355
(227, 128)</td><td>35%</td><td>20%</td><td>86%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
<tr><td rowspan="2">66%</td><td rowspan="2">368
(243, 125)</td><td>35%</td><td>20%</td><td>84%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
<tr><td rowspan="2">68%</td><td rowspan="2">380
(258, 122)</td><td>35%</td><td>20%</td><td>85%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
<tr><td rowspan="2">70%</td><td rowspan="2">400
(280, 120)</td><td>35%</td><td>20%</td><td>84%</td></tr>
<tr><td>40%</td><td>25%</td><td>81%</td></tr>
</table></td><td>Replaced the original sample size table with the updated table presented to the DSMB at the April 21, 2017 meeting.</td></tr>
<tr><td>5.3.1. Interim Analysis for Efficacy</td><td>5.3.1. Interim Analysis for Efficacy</td><td>Analyses will be performed as described below for the primary endpoint. At the time of each interim analysis, a two-sided test to detect either an increase or decrease in the proportion of patients surviving will be performed. The test statistics will be based on the Kaplan-Meier proportions, which have independent increments as described by</td><td>Analyses will be performed as described below for the primary endpoint. At the time of each interim analysis, a two-sided test to detect either an increase or decrease in the proportion of patients surviving will be performed. The test statistic used at each interim analysis will be the difference between treatment arms in adjusted estimates of three year overall survival.</td><td>Clarification that interim analyses for the primary endpoint will use covariate-adjusted survival probability estimates.</td></tr>
</table>

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		Gu et al[40]. All patients enrolled prior to the time of the interim analyses will be used to compute the Kaplan-Meier estimate of overall survival at three years. If the test statistic exceeds the critical value, the DSMB will discuss whether the trial should continue.	All patients enrolled prior to the time of the interim analyses will be used to compute these adjusted probability estimates. If the test statistic exceeds the critical value, the DSMB will discuss whether the trial should continue.	
5.3.1. Interim Analysis for Efficacy	5.3.1. Interim Analysis for Efficacy	In order to preserve the overall Type I error rate at 5%, the critical value for the test statistic will be inflated above 1.96, the value that would be used if no repeated testing were used. Equivalently, the nominal p-value at which an observed difference is declared significant will be reduced below 0.05. The actual critical values and nominal p-values will be computed using statistical methods for group sequential testing with O'Brien Fleming boundaries. Information is defined as the reciprocal of the variance of the difference in Kaplan-Meier estimates between the two treatments. If there is no censoring prior to three years, the final information at the end of the study reduces to the reciprocal of the variance of the difference in two binomial proportions. The information time used in the power calculations were estimated from a simulation study with 1000 replicates assuming 10% censoring prior to three years and assuming the survival	In order the preserve the overall Type I error rate at 5%, the critical value for the test statistic will be inflated above 1.96, the value that would be used if no repeated testing were used. Equivalently, the nominal p-value at which an observed difference is declared significant will be reduced below 0.05. The actual critical values and nominal p-values will be computed using statistical methods for group sequential testing with Haybittle-Peto boundaries[ii,iii]. Because differences in adjusted survival estimates are not known to follow an independent increments structure asymptotically, a Bonferroni adjustment will be used to ensure that the overall type I error rate does not exceed 0.05. Letting K denote the total number of analyses and π_j the nominal type I error rate for the analysis performed at analysis j, the overall type I error rate will not exceed 0.05 if these are chosen such that $\sum_{j=1}^{K} \pi_j = 0.05$. The Haybittle-Peto design uses a critical value of 3.00 at each	Explanation of the methods used for the interim analyses. The stopping boundaries / critical values used are listed. Removed reference to information level, since Haybittle-Peto designs do not use it.

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		time and censoring time are independent. The information fraction is the ratio of the information at an interim analysis to the final information at the end of the study.	intermediate analysis, giving $\pi_j = 2[1 - \Phi(3)] = 0.0027$ for stages $j < K$ and $\pi_K = 0.05 - 2(\mathrm{K} - 1)[1 - \Phi(3)]$ for the final analysis, where Φ is the standard normal cumulative distribution function. The critical value for the final analysis, then, is $\Phi^{-1}(1 - \pi_K/2)$.	
5.3.1. Interim Analysis for Efficacy	5.3.1. Interim Analysis for Efficacy	We recommend interim analyses starting four years after the beginning of the study and yearly thereafter, until the last patient has been followed for three years. Four years was chosen as the time of the first interim analysis to ensure enough patients have reached the primary endpoint to provide reasonable estimate of three-year survival. The number of subsequent analyses depends on length of time required to complete accrual. The final information required to achieve at least 80% power to detect a 15% difference in three-year survival probabilities between treatment arms with a two-sided type I error of 5% was estimated to be 348.84.	We recommend interim analyses starting four years after the beginning of the study and yearly thereafter, until the last patient has been followed for three years. Four years was chosen as the time of the first interim analysis to ensure enough patients have reached the primary endpoint to provide reasonable estimates of three-year survival. The number of subsequent analyses depends on the length of time required to complete accrual.	Removed reference to information level, since it is not required for Haybittle-Peto boundaries.
5.3.1. Interim Analysis for Efficacy	5.3.1. Interim Analysis for Efficacy	Assuming donor availability rate of 60%, the total accrual time is estimated to be 2.5 years. With 3 years of follow up, the study can be completed within 6 years. In this case, analyses will be conducted at the end of year 4, 5, and 6. As an example, Table 5.3.A shows the critical values, nominal Type I error, cumulative	Assuming donor availability rate of 60%, the total accrual time is estimated to be 2.5 years. With 3 years of follow up, the study can be completed within 6 years. In this case, analyses will be conducted at the end of year 4, 5, and 6. Table 5.3.A shows the critical values, nominal Type I error, cumulative Type I error, and the	Added details on how simulations were conducted. Updated power estimates under the modified design.

<table>
<tr><th>Section number and title in Version 4.0</th><th>Section number and title in Amendment</th><th>Original Text</th><th>Changed To</th><th>Rationale</th></tr>
<tr><td></td><td></td><td>Type I error, and the probability of stopping to reject the null hypothesis at each analysis conducted at the end of year 4, 5, and 6. The power at each look is the probability of stopping and rejecting the null hypothesis at that look if the true increase in OS at three years is 15% in the HCT arm compared to the non-HCT arm. In particular, there is 47% power to detect a 15% improvement in three-year survival by the first look, 76% by the second look, and 83% by the final look if the true survival probabilities were 35% vs. 20%. There is 43% power to detect the same improvement by the first look, 72% by the second look, and 80% power by the final look if the true survival probabilities were 40% vs. 25%.</td><td>probability of stopping to reject the null hypothesis at each analysis conducted at the end of year 4, 5, and 6. This is estimated using a simulation study with two different survival probability scenarios, uniform accrual over 2.5 years, and assuming exponential censoring with 10% rate by 3 years; we use an unadjusted test statistic for simulation study purposes, even though the primary analysis will use the difference in adjusted survival probabilities at 3 years. The power at each look is the probability of stopping and rejecting the null hypothesis at that look if the true increase in OS at three years is 15% in the HCT arm compared to the non-HCT arm. In particular, there is 32% power to detect a 15% improvement in three-year survival by the first look, 51% by the second look, and 83% by the final look if the true survival probabilities were 35% vs. 20%. There is 29% power to detect the same improvement by the first look, 46% by the second look, and 79% power by the final look if the true survival probabilities were 40% vs. 25%.</td><td></td></tr>
<tr><td>TABLE 5.3.A: CRITICAL VALUES AND OPERATING CHARACTERISTICS</td><td>TABLE 5.3.A: CRITICAL VALUES AND OPERATING CHARACTERISTICS; DONOR</td><td><table>
<tr><th rowspan="2">Calendar Time since Study Start</th><th rowspan="2">Information Fraction</th><th rowspan="2">Critical Value</th><th rowspan="2">Nominal Type I Error</th><th rowspan="2">Cumulative Type I Error</th><th colspan="2">Cumulative Probability of Stopping under H_0</th></tr>
<tr><th>35% vs. 20%</th><th>40% vs. 25%</th></tr>
<tr><td>4 years</td><td>0.67</td><td>2.50</td><td>.0124</td><td>.0124</td><td>.4738</td><td>.4332</td></tr>
<tr><td>5 years</td><td>0.90</td><td>2.14</td><td>.0326</td><td>.0363</td><td>.7606</td><td>.7224</td></tr>
<tr><td>6 years</td><td>1.00</td><td>2.07</td><td>.0388</td><td>.0500</td><td>.8347</td><td>.8020</td></tr>
</table></td><td><table>
<tr><th rowspan="2">Calendar Time since Study Start</th><th rowspan="2">Critical Value</th><th rowspan="2">Nominal Type I Error Rate</th><th rowspan="2">Cumulative Type I Error Rate Upper Bound</th><th colspan="2">Cumulative Probability of Stopping under H_0</th></tr>
<tr><th>35% vs. 20%</th><th>40% vs. 25%</th></tr>
<tr><td>4 years</td><td>3.00</td><td>0.0027</td><td>0.0027</td><td>0.3238</td><td>0.2892</td></tr>
<tr><td>5 years</td><td>3.00</td><td>0.0027</td><td>0.0054</td><td>0.5096</td><td>0.4562</td></tr>
<tr><td>6 years</td><td>2.01</td><td>0.0446</td><td>0.0500</td><td>0.8272</td><td>0.7906</td></tr>
</table></td><td>Updated operating characteristics under the modified design.</td></tr>
</table>

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	AVAILABILITY RATE OF 60%			
5.3.1. Interim Analysis for Efficacy	5.3.1. Interim Analysis for Efficacy	Assuming donor availability rate of 70%, the total accrual time is estimated to be 3.5 years. With 3 years of follow up, the study can be completed within 7 years. In this case, analyses will be conducted at the end of year 4, 5, 6, and 7. As an example, Table 5.3.B shows the critical values, nominal and cumulative Type I error, and the power to reject the null hypothesis by each look conducted at the end of year 4, 5, 6, and 7. In particular, there is 65% power to detect a 15% improvement in three-year survival by the second look and 84% by the final look if the true survival probabilities were 35% vs. 20%. There is 61% power to detect the same improvement by the second look and 81% power by the final look if the true survival probabilities were 40% vs. 25%.	Assuming donor availability rate of 70%, the total accrual time is estimated to be 3.5 years. With 3 years of follow up, the study can be completed within 7 years. In this case, analyses will be conducted at the end of year 4, 5, 6, and 7. Table 5.3.B shows the critical values, nominal and cumulative Type I error, and the power to reject the null hypothesis by each look conducted at the end of year 4, 5, 6, and 7. This is estimated using a simulation study with two different survival probability scenarios, uniform accrual over 3.5 years, and assuming exponential censoring with 10% rate by 3 years; we use an unadjusted test statistic for simulation study purposes, even though the primary analysis will use the difference in adjusted survival probabilities at 3 years. In particular, there is 46% power to detect a 15% improvement in three-year survival by the second look and 85% by the final look if the true survival probabilities were 35% vs. 20%. There is 41% power to detect the same improvement by the second look and 81% power by the final look if the true survival probabilities were 40% vs. 25%.	Added details on how simulations were conducted. Updated power estimates under the modified design.

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<tr><td>TABLE 5.3.B: CRITICAL VALUES AND OPERATING CHARACTERISTICS</td><td>TABLE 5.3.B: CRITICAL VALUES AND OPERATING CHARACTERISTICS; DONOR AVAILABILITY RATE OF 70%</td><td><table>
<tr><th rowspan="2">Calendar Time since Study Start</th><th rowspan="2">Information Fraction</th><th rowspan="2">Critical Value</th><th rowspan="2">Nominal Type I Error</th><th rowspan="2">Cumulative Type I Error</th><th colspan="2">Cumulative Probability of Stopping under H_0</th></tr>
<tr><th>35% vs. 20%</th><th>40% vs. 25%</th></tr>
<tr><td>4 years</td><td>0.53</td><td>2.86</td><td>.0042</td><td>.0042</td><td>.2444</td><td>.2193</td></tr>
<tr><td>5 years</td><td>0.79</td><td>2.29</td><td>.0220</td><td>.0234</td><td>.6461</td><td>.6081</td></tr>
<tr><td>6 years</td><td>0.94</td><td>2.12</td><td>.0338</td><td>.0409</td><td>.7905</td><td>.7579</td></tr>
<tr><td>7 years</td><td>1.00</td><td>2.09</td><td>.0366</td><td>.0500</td><td>.8355</td><td>.8063</td></tr>
</table>
To permit necessary flexibility in scheduling interim analyses, the critical values will be recomputed to correspond to the actual available statistical information using the “use-function” approach of Lan and DeMets.</td><td><table>
<tr><th rowspan="2">Calendar Time since Study Start</th><th rowspan="2"></th><th rowspan="2">Nominal Type I Error Rate</th><th rowspan="2">Cumulative Type I Error Rate Upper Bound</th><th colspan="2">35% vs. 20%</th><th colspan="2">40% vs. 25%</th></tr>
<tr></tr>
<tr><td>4 years</td><td>3.00</td><td>0.0027</td><td>0.0027</td><td>0.2538</td><td>0.2226</td></tr>
<tr><td>5 years</td><td>3.00</td><td>0.0027</td><td>0.0054</td><td>0.4564</td><td>0.4058</td></tr>
<tr><td>6 years</td><td>3.00</td><td>0.0027</td><td>0.0081</td><td>0.5636</td><td>0.5124</td></tr>
<tr><td>7 years</td><td>2.03</td><td>0.0419</td><td>0.0500</td><td>0.8476</td><td>0.8084</td></tr>
</table></td><td>Updated operating characteristics under the modified design. Removed reference to a use function, since the modified design does not use it.</td></tr>
<tr><td>5.5.1. Analysis of the Primary Endpoint</td><td>5.5.1. Analysis of the Primary Endpoint</td><td>The primary outcome of the trial is overall survival at three years after consent. The primary null hypothesis of the study is that there is no difference in overall survival between the treatment arms at three years post consent. In the primary analysis, the intent-to-treat principle will be used. Because of the potential bias resulting from biological assignment[iv], the comparisons of overall survival will be adjusted for the following pre-specified patient characteristics: age, race/ethnicity, performance status, disease status, co-morbidity index, IPSS score, duration of disease (time from diagnosis to enrollment), cytogenetics, and response to prior therapy. The primary analysis will be performed using the difference in adjusted overall survival probabilities at three years, using the method of Zhang et</td><td>The primary outcome of the trial is overall survival at three years after consent. The primary null hypothesis of the study is that there is no difference in overall survival between the treatment arms at three years post consent. In the primary analysis, the intent-to-treat principle will be used. Because of the potential bias resulting from biological assignment[vi], the comparisons of overall survival will be adjusted for the following pre-specified patient characteristics: age, race/ethnicity, performance status, disease status, co-morbidity index, IPSS score, duration of disease (time from diagnosis to enrollment), cytogenetics, and response to prior therapy. The primary analysis will be performed using the difference in adjusted overall survival probabilities at three years, using the method of Zhang et al[i]. In this</td><td>Clarified that the event time of interest is the time of death, which may be censored.</td></tr>
</table>

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		al[v]. In this analysis, the time to event is the time from study consent to the time of death or last follow-up whichever occurs first, and the adjusted survival probabilities are estimated using the Cox proportional hazards model stratified by treatment. A 95% confidence interval for the difference in adjusted OS at three years will also be constructed. In addition to a point-wise comparison at three years, adjusted survival curves will be constructed and confidence bands for the difference between treatments will be generated to compare the survival probabilities across time.	analysis, the time to event is the time from study consent to the time of death from any cause; surviving patients will be censored at last follow-up. The adjusted survival probabilities are estimated using the Cox proportional hazards model stratified by treatment. A 95% confidence interval for the difference in adjusted OS at three years will also be constructed. In addition to a point-wise comparison at three years, adjusted survival curves will be constructed and confidence bands for the difference between treatments will be generated to compare the survival probabilities across time.	
APPENDIX B: Informed Consent to Participate in Research Section 10. Privacy, Confidentiality and Use of Information	APPENDIX B: Informed Consent to Participate in Research Section 10. Privacy, Confidentiality and Use of Information	--	Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are. Data regarding your clinical situation, including follow-up after 3-4 years, may be obtained from the CIBMTR, which captures information on all US transplants.	Language was added to all BMT CTN protocols regarding the Certificate of Confidentiality and CIBMTR data reporting.

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<tr><td>APPENDIX E: INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS) AND REVISED INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS-R) FOR PATIENTS WITH MDS</td><td>APPENDIX E: INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS) AND REVISED INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS-R) FOR PATIENTS WITH MDS</td><td>
<table>
<tr><th>Risk Group</th><th>IPSS Score</th></tr>
<tr><td>Low</td><td>0</td></tr>
<tr><td>Intermediate - 1</td><td>0.5 - 1.0</td></tr>
<tr><td>Intermediate - 2</td><td>1.5 - 2.0</td></tr>
<tr><td>High</td><td>> 2.5</td></tr>
</table>
</td><td>
<table>
<tr><th>Risk Group</th><th>IPSS Score</th></tr>
<tr><td>Low</td><td>0</td></tr>
<tr><td>Intermediate - 1</td><td>0.5 - 1.0</td></tr>
<tr><td>Intermediate - 2</td><td>1.5 - 2.0</td></tr>
<tr><td>High</td><td>≥ 2.5</td></tr>
</table>
</td><td>It was clarified that patients with an IPSS score of 2.5 should be classified as ‘High Risk’.</td></tr>
</table>

[i] Zhang X, Loberiza FR, Klein JP, and Zhang, MJ. A SAS macro for estimation of direct adjusted survival curves based on a stratified Cox regression model. Computer Methods and Programs in Biomedicine 2007; 88: 95-101.

[ii] Haybittle JL. Repeated assessment of results in clinical trials of cancer treatment. British Journal of Radiology. 1971, 44(526):793-7.

[iii] Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. I. Introduction and design. British Journal of Cancer. 1976, 34(6):585.

[iv] Logan B, Leifer E, Bredeson C, Horowitz M, Ewell M, Carter S, et al. Use of biological assignment in hematopoietic stem cell transplantation clinical trials. Clinical Trials. 2008;5(6):607-1

[v] Zhang X, Loberiza FR, Klein JP, and Zhang, MJ. A SAS macro for estimation of direct adjusted survival curves based on a stratified Cox regression model. Computer Methods and Programs in Biomedicine 2007; 88: 95-101.

[vi] Logan B, Leifer E, Bredeson C, Horowitz M, Ewell M, Carter S, et al. Use of biological assignment in hematopoietic stem cell transplantation clinical trials. Clinical Trials. 2008;5(6):607-1