BLOOD AND MARROW
TRANSPLANT
CLINICAL TRIALS NETWORK

BMT CTN 1401/ MYELOMA VACCINE

PHASE II MULTICENTER TRIAL OF SINGLE AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANT FOLLOWED BY LENALIDOMIDE MAINTENANCE FOR MULTIPLE MYELOMA WITH OR WITHOUT VACCINATION WITH DENDRITIC CELL/MYELOMA FUSIONS

NCT#: NCT02728102

Statistical Analysis Plan

Version 1.0

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BMT CTN Protocol 1401 Statistical Analysis Plan (SAP)

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Prepared by: Print Name: Maggie Wu
Signature:

Date: 01JUL2019

Protocol Statistician

Reviewed by: Print Name: Brent Logan
Signature:

Date: 09JUL2019

BMT CTN DCC Statistician Leadership

Approved by: Print Name: Marcelo Pasquini
Signature:

Date: 7/9/2019

Protocol Chair/Protocol Officer

07/JUL/2019

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Protocol

BMT CTN #1401 is titled “Phase II Multicenter Trial of Single Autologous Hematopoietic Cell Transplant Followed by Lenalidomide Maintenance for Multiple Myeloma with or without Vaccination with Dendritic Cell/Myeloma Fusions”.

1. General Review of Study Design and Process

1.1 Study Objectives

BMT CTN protocol #1401 is a three-arm, Phase II, open-labeled, multi-center trial designed to evaluate whether dendritic cell (DC)/myeloma fusion vaccine in combination with granulocyte macrophage colony-stimulating factor (GM-CSF) and standard immunomodulatory therapy, i.e. lenalidomide, can be used as an upfront cellular immunotherapy following autologous transplant for participants with multiple myeloma[1]. Primarily, the study aims to identify whether the combination of vaccine and maintenance therapy increases post-transplant clinical response compared to the non-vaccine control groups (lenalidomide with and without GM-CSF). Furthermore, the study will assess the effect of the vaccine on the anti-myeloma immunity by isolating the effect of lenalidomide maintenance and/or GM-CSF adjuvant.

1.1.1 Primary Objective

The primary objective of the study is to compare the percentage of participants alive and achieving complete response (CR) or stringent complete response (sCR) at one year post transplant (approximately 10 months post randomization) between participants randomized to the vaccine arm and participants randomized to the combined non-vaccine arms (lenalidomide with/without GM-CSF).

1.1.2 Secondary Objectives

The secondary objectives of the study include:

- Myeloma response to treatment
- Cumulative incidence of myeloma progression
- Cumulative incidence of treatment-related mortality (TRM)
- Progression-free survival (PFS)
- Overall survival (OS)
- Incidence of grade ≥ 3 toxicities per CTCAE version 4.0
- Incidence of infection
- Minimal residual disease assessment

1.1.3 Exploratory (immunologic) Objectives

The exploratory (immunologic) objectives of the study are/include:

- Myeloma-reactive T-cells

- Assessment of antigen-specific reactivity
- Quantification of T-cell subsets
- Assessment of effect on NK cell population
- Assessment of humoral immune response

1.2 Study Design and Procedures

1.2.1 Primary Hypothesis and Primary Endpoint

The primary hypothesis of the study is that vaccination with DC/myeloma fusions/GM-CSF in combination with lenalidomide maintenance therapy will increase the proportion of participants alive and in CR or sCR at one year post transplant compared to the combined non-vaccine groups.

$$H0: P_{VACCINE/GMCSF+MAINT} = P_{MAINT\pm GMCSF} \text{ vs. } Ha: P_{VACCINE/GMCSF+MAINT} > P_{MAINT\pm GMCSF}.$$

The primary endpoint is the proportion of participants alive and in CR or sCR at one year post transplant (corresponding to approximately 10 months post randomization).

1.2.2 Accrual Plan and Randomization

The study targets 132 randomized participants. Considering 30% of participants are expected to drop out between tumor cell collection and randomization, the study will target 188 participants for tumor cell collection. It was estimated that 36 months of accrual will be necessary to enroll the target sample size.

Participants will be randomized to DC/myeloma vaccine/GM-CSF/lenalidomide, lenalidomide/GM-CSF, and lenalidomide alone in a 2:1:1 ratio using random block sizes. Randomization will be stratified based on disease response at time of randomization between stringent complete response/complete response and very good partial response/partial response/stable disease.

A memorandum was issued on August 1, 2018 to the participating sites of this trial regarding the Accrual Continuation Plan that the study enrollment will remain open until enrollment reached 203 patients with tumor cell collection. This change was intended to ensure sufficient patients proceed to randomization given a higher than expected drop-off rate and the long period between tumor cell collection and randomization. The expanded accrual was noted in the Data and Safety Monitoring Board (DSMB) and FDA reports.

1.2.3 Duration of Follow-up

Participants will be followed for approximately 3 years post maintenance initiation for AE (including SPM). The primary endpoint is at 1 year post transplant. Secondary endpoints data are collected from Emmes end up to approximately 2 years (through cycle 24 of maintenance).

Data regarding study participants' clinical situation, including follow-up after 2 years, may be obtained from the Center for International Blood and Marrow Transplant Research (CIBMTR), which captures information on all US transplants. Such long-term follow-up data is NOT within the scope of this SAP and analysis on these long-term follow up data is not part of the primary analysis.

1.3 Inclusion/Exclusion Criteria and Treatment Description

Patients must be considered transplant eligible by treating physician at the time of study. Patients will be enrolled prior to tumor cell collection for vaccine manufacturing. Eligible patients are ≥18.00 and < 71.00 years of age with symptomatic multiple myeloma requiring treatment, without history of prior disease progression or prior HCT, Karnofsky performance score ≥70%, evidence of at least 20% plasma cells in a bone marrow differential within 60 days of enrollment and have received <1 cycle of systemic anti-myeloma therapy. If patient receives anti-myeloma therapy treatment after bone marrow aspirate to assess eligibility and before bone marrow aspirate for tumor cell collection, a repeat bone marrow evaluation will be required to confirm > 20% plasma cells in the bone marrow aspirate differential prior to enrollment and tumor cell collection. Patients with prior auto or allo transplant are not eligible. Patients with active autoimmune diseases will be excluded. More details for inclusion and exclusion criteria for study enrollment are outlined in Protocol Version 4.0 Chapter 2.3.2.

Randomization eligibility will be evaluated prior to randomization among transplanted participants. In order to be randomized to study treatments (maintenance therapy), participants are required to have sufficient tumor cells and subsequent vaccine production with no evidence of disease progression within 10 days prior to randomization, a minimum of 75,000/mm^3 for platelet count without transfusion in previous 7 days and a minimum of 1,500/mm^3 for absolute neutrophil count without filgrastim administration within 7 days or pegfilgrastim within 14 days of measurement, and maintain adequate physical function measured by hepatic and renal assessments. Details are documented in Protocol Version 4.0 Chapter 2.3.3.

Amendments to eligibility criteria since the first version of the protocol release Version 1.0 were documented in the protocol amendment summary of changes.

1.4 Treatment Description

Eligible participants will undergo tumor cell collection after enrollment. Participants with bone marrow harvest that yields sufficient cell counts per BMT CTN 1401 Vaccine Product Release Criteria will be scheduled for an autologous hematopoietic cell transplant within 1 year of enrollment. Pre-transplant systemic anti-myeloma therapy will be administered per institutional practices. Transplant-eligible participants will receive an autologous graft with a minimum cell dose of 2.0 x 10^6 CD34+ cells/kg with high-dose melphalan (200mg/m^2).

A disease response assessment will be done approximately 2 months post-transplant and participants who meet eligibility criteria will be randomized within 10 days of the

assessment to one of three treatment groups: vaccine/GM-CSF with lenalidomide, lenalidomide/GM-CSF, or lenalidomide alone.

Participants start maintenance therapy between 90 and 100 days post-transplant (approximately 1 month post randomization). Lenalidomide will be administered at an initial dose of 10 mg per day starting Day 1 for 2 years (24 maintenance therapy cycles) until disease progression. One maintenance therapy cycle lasts for 28 days and participants will be only given a 28-day supply at a time. The dose modifications for lenalidomide are described in Protocol Version 4.0 Chapter 2.4.6. Participants who are randomized to the vaccine arm will receive 3 doses of the vaccine on the first day of 2nd, 3rd, and 4th cycle of lenalidomide with an injection of GM-CSF on the same day and every day for 3 days after the vaccine to boost the effect of the vaccine. Participants who are randomized to the lenalidomide/GM-CSF arm will receive GM-CSF injection every day for 4 days starting the first day of 2nd, 3rd, and 4th cycle of lenalidomide.

1.5 Response Variables and Data Collection Time Points

1.5.1 Response Variables

The response variables for this study include the primary, secondary, safety and immunologic endpoints. The primary endpoint is the proportion of participants alive with CR/sCR at 1 year post transplant (approximately 10 month post maintenance initiation).

Secondary endpoints include:

- Disease response/myeloma response to treatment
- Disease progression/myeloma progression
- Treatment-related mortality
- Progression-free survival
- Overall survival
- Minimal residual disease

Immunologic endpoints include:

- The percent of participants achieving at least a 2.4-fold increase in myeloma-specific T cells from pre-therapy to peak post-treatment levels
- The percent of participants achieving at least a 10-fold increase in myeloma-reactive T-cells
- Assessment of antigen specific reactivity in HLA-A2.1 participants by multichannel flow cytometry and intracellular staining
- Quantification of T-cell subsets by multichannel flow cytometry
- Assessment of effect of lenalidomide alone and in combination with vaccination on the phenotype and function of NK cell populations

- Assessment of humoral response targeting myeloma antigens in participants treated with lenalidomide alone and in combination with vaccination

Safety endpoints included mortality, toxicity and adverse events. Safety monitoring will be conducted per protocol schedule. Adverse events will be reported per the BMT CTN Manual of Procedures (MOP).

Definitions for each endpoint are described in detail in Protocol Version 4.0 Chapter 3 and in Section 3 of this SAP.

1.5.2 Timing of Assessments

Participants are evaluated for pre-enrollment assessments at study entry. Pre-enrollment evaluations must be determined within 8 weeks prior to enrollment. Bone marrow aspirate and biopsy are required to assess plasma cell involvement within 60 days of enrollment. Once participants enter the study, tumor cell collection will be done for vaccine production and randomization eligibility validation. Initiation of systemic anti-myeloma therapy and transplant will be done within 1 year of enrollment to the study. Participants who are unable to have tumor cell collection or vaccine preparation done appropriately per BTM CTN 1401 manufacturing SOP may still receive initial anti-myeloma therapy and transplant but will be dropped from the study and not proceed to transplant.

Participants who undergo autologous hematopoietic cell transplant will be seen 14 days or less prior to randomization for pre-randomization evaluations, and disease response assessment must be performed within 10 days prior to randomization. Randomization occurs approximately 2 months post-transplant (from Day 53 to Day 90). Before starting the assigned maintenance therapy, participants need to complete pre-maintenance evaluations within 14 days prior to initiation of lenalidomide for eligibility. Post maintenance initiation assessments including toxicities, bone marrow evaluation, laboratory disease evaluation, and physical function occur monthly for the first 4 cycles, and then at cycles 6, 9, 12, 15, 18, 21, and 24. One maintenance cycle duration is 28 days. Disease response will be assessed at 6 months, 1 year, and 2 years post-transplant. Participants who stop maintenance therapy for any reason will still be followed on the study, unless they withdraw consent from the study.

Sample collection for ancillary studies and for future research use are performed at enrollment, pre-randomization, and during maintenance. Death, relapse, infections, hospitalizations, and adverse events are reported on event-driven forms. Data on occurrence of these events are recorded per the BMT CTN MOP.

Participant data related to primary and secondary endpoints are collected through AdvantageEDC up to 28 days after the last maintenance dose or 2-year post-transplant depending on participant's compliance to the lenalidomide. The specimens collected for immunologic endpoints are being tracked in AdvantageEDC and Global Trace. Samples will be shipped to BMT CTN Biorepository or institutional laboratories based on the purpose of specimen. All unexpected grades 3-5 AEs unless a participant has protocol-

defined progression, and second primary malignancies (SPM) regardless of progression are required to be reported using the expedited AE reporting system in AdvantageEDC through 3-year post maintenance. Other follow up data after 2 years post maintenance initiation until 3 years post maintenance initiation will be obtained from the CIBMTR.

2. General Statistical Considerations

2.1 Sample Size and Power Calculations

The primary hypothesis testing will be done using a one-sided two-sample comparison of proportions between the vaccine arm and the combined non-vaccine arms. The prior studies suggest a 29% and 54% CR rate respectively at 100 days and 1 year post transplant for participants who undergo post-transplant vaccination in the absence of lenalidomide maintenance. Thus, it's anticipated that 40% of study participants will achieve CR/sCR at 1 year post transplant following vaccination without lenalidomide maintenance. Considering lenalidomide maintenance therapy will boost the effects of vaccination and thus enhance vaccine efficacy[2], we will consider vaccine/GM-CSF plus lenalidomide therapy to be promising if there is a 20% increase in CR rate at 1 year from 40% to 60%. For the primary comparison between the vaccine and the combined non-vaccine arms, 66 participants in each group is sufficient to maintain a one-sided type I error rate of 10% and provide 85% statistical power to detect a 20% improvement in the 1 year CR rate using a two-sample proportions test. Furthermore, since randomization occurs after tumor cell collection and transplant, we expect a 30% drop-out rate and thus the study planned to enroll a total of 188 participants at the time of initial tumor collection (later expanded to 203 participants).

In a secondary pairwise analysis that compares CR rate at 1 year post transplant between the vaccine arm versus either lenalidomide/GM-CSF arm or lenalidomide only arm, the sample size (66 in the vaccine arm, 33 in each non-vaccine arm) is also sufficient to detect a 23% increase while maintaining a 80% power under the same alpha level. Besides, a 26% increase between the two non-vaccine groups can also be detected with 80% power.

Since this is a Phase II trial, the consideration on sample size and power calculation and study design of the trial is not intended to provide definitive results but rather to detect any promising difference in response rates between the vaccine arm and combined non-vaccine arm by assessing vaccination plus maintenance therapy in a multi-center setting for future trials consideration.

2.2 Handling Missing Data

Comprehensive data quality assurance will be conducted to reconcile data issues including missing data.

The primary endpoint will be evaluated at 1 year post-transplant (approximately 10 months post randomization). An Endpoint Review Committee (ERC) will adjudicate the primary endpoint and resolve this endpoint for any participants with missing data using

available source documents provided by sites. Remaining participants with missing data will be considered not evaluable.

For time-to-event variables, participants will be censored at the last observation for the endpoint if they have not had an event or competing risk event. Participants lost to follow-up will be censored at the time of last contact date captured in the AdvantageEDC.

Since this is a phase II trial, all available data will be used in the analyses and no imputation will be done on missing data.

2.3 Multiple Comparisons

A one-sided significance level of 10% will be used for testing the primary endpoint between the vaccine group and combined non-vaccine groups. The same alpha level will be used for the secondary comparisons of CR rate between the vaccine versus either lenalidomide/GM-CSF or lenalidomide alone arm. All other secondary analyses will use a two-sided significance level of 5%. The pairwise tests for treatment group difference that compare 2 groups at a time will use the 0.05 significance level, but these comparisons will only be considered significant if the multiple degree of freedom overall test among the three groups is significant.

2.4 Interim Analysis

No interim analyses for efficacy or futility were planned for the study.

The key safety endpoint for interim monitoring is the treatment limiting toxicity (TLT) within the first month of the combined therapy. TLT will be monitored separately for the vaccine/GM-CSF arm and the combined non-vaccine groups (lenalidomide/GM-CSF arm and lenalidomide alone arm) under the same stopping rule using a truncated SPRT for binary outcomes. Each month, the null hypothesis that the 1 month TLT rate is 25% will be tested. At each interim analysis, the total number of participants enrolled and started combined therapy is plotted against the total number of participants who have experienced TLT. The continuation region of the SPRT[3] is defined by two decision boundaries. Only the upper boundary will be used for monitoring the study to protect against high incidences of TLT. If the graph falls above the upper boundary, the SPRT rejects the null hypothesis, and concludes that the TLT incidence is higher than predicted by the observed number of participants enrolled on study. Otherwise, the SPRT continues until enrollment reaches the target goal. The SPRT for TLT was developed from the following SPRT:

A SPRT contrasting 25% versus 40% 1 month incidence, with nominal type I and II errors of 12% and 15%, respectively, which results in decision boundaries with a common slope of 0.322 and an upper intercept of 2.824.

The table illustrates the operating characteristics of the described truncated test based on a simulation study that assumed uniform accrual of 66 individuals over a three-year

time period. When the true 1 month incidence rate is 25%, 10% of the time we will reject the null hypothesis. When the true rate is 40%, there is an 84% chance of rejecting the null hypothesis.

True 1 month Incidence	25%	35%	40%	45%
Probability Reject Null	0.100	0.595	0.836	0.957
Mean Month Stopped	34.8	25.0	18.3	13.5
Mean # Endpoints in 1 month	15.5	15.4	13.1	10.6
Mean # Participants Enrolled	62.1	43.8	32.7	23.7

2.5 Timing of Analysis

The first round of the analysis is the timing for the primary endpoint, which is when all participants complete one year follow-up post-transplant and the ERC completes the endpoint adjudications on the primary endpoint.

A topline analysis will be conducted to include the primary clinical endpoint, primary immunologic endpoint and some secondary endpoints to facilitate abstract submission of the primary results. For the secondary endpoints, this topline analysis will only include descriptive analysis on the secondary endpoints with 1-year data but no formal comparison will be conducted in order to maintain planned statistical power when final data become available. Secondary endpoints in the topline analysis will only include disease response, disease progression, treatment-related mortality, progression-free survival, overall survival, and all these will only include data within 1 year. Study enrollment, patient demographics and baseline data will also be included in the topline analysis.

A data freeze will be done upon the completion of ERC adjudication on the primary endpoint and completion of related data quality assurance. An ERC Charter will be in place to define the scope of ERC review as well as the timeline for the data adjudication.

The second round of the analysis is the timing for all the secondary endpoints with complete 2-year follow-up. A comprehensive analysis report including 2-year data for primary endpoint and all secondary endpoints is planned when the last randomized participant finishes 2-year post maintenance assessment. The comprehensive analysis is conducted to facilitate the primary manuscript submission of the study. Correlative immunologic endpoints that defined in the protocol will be included in this comprehensive analysis report. Emmes will request data from study labs and run analyses per protocol.

Analysis on the long-term follow up beyond 2-year post maintenance are not collected in AdvantageEDC Emmes data system and will be collected via the CIBMTR data system. This will be a separate publication and the analysis plan are not covered in this SAP.

The timing for the ancillary studies, the T Cell/Genomic Signature and the VCAN Proteolysis, are covered in separate protocols managed by the Beth Israel Deaconess Medical Center and University of Wisconsin-Madison respectively. Analysis plans for these ancillary studies are not covered in this SAP.

2.6 Software

All analyses will be conducted using SAS 9.4 or higher software, or R version 3.4.4 or higher.

2.7 Analysis Populations

2.7.1 Enrolled Population

All participants who were enrolled to the study will be counted in the enrolled population. Participants who did not make it to randomization due to various reasons will be described.

2.7.2 Primary Analysis Population

All randomized participants will be included in the primary analysis population per intent-to-treat (ITT) principle regardless of whether the assigned transplant was administered. This population will be applied to the primary endpoint and some secondary endpoints. It is clearly defined for each secondary endpoint whether or not this population will be used for analysis, as described in section 3.2 of this SAP.

2.7.3 Safety Analysis Population

The reporting of serious adverse events will be consistent with standard BMT CTN procedures and compliant with additional requirements from Celgene Corporation who supplies lenalidomide for the study with the addition of any anticipated SAE related to the study drug or treatment/procedure. All reported serious adverse events potentially associated with study drug or treatment/procedure will be carefully examined with respect to the severity and relationship to study drug. The type and severity of adverse events will be described. Safety data will be summarized using Medical Dictionary for Regulatory Activities (MedDRA) Coding Version 20.0 or above.

All secondary primary malignancies (SPMs), excluding non-melanoma skin cancers, experienced by participants from the time of enrollment until 3 years post maintenance initiation will also be reported.

The safety analysis population will consist of participants according to treatment received and SPM analysis population will consist of all enrolled participants.

2.8 General Analysis Guidelines

Continuous variables will be described using mean, standard deviation, median, quartiles, minimum and maximum. Frequencies and percentages will be displayed for categorical data. The log transformation will be applied to immunological endpoints to induce normality in quantitative measurements. Between group comparisons will be

performed for continuous variables via a Kruskal-Wallis test and for categorical variables, via the chi-squared test.

Any changes to the planned analyses and ad hoc analysis will be documented in the final analysis report with detailed justifications. If it is a change to analysis of an existing endpoint, the change should be clearly stated in the relevant exhibit. If it is a new endpoint or analysis performed, it should be included in a supplemental exhibit.

Statistical consideration and analysis plan for the ancillary studies will be handled by separate study teams thus not covered in this SAP.

2.9 Demographics and Baseline Characteristics

Descriptive statistics for demographics and baseline characteristics will be presented by treatment group. Characteristics to be examined are: age, gender, race, ethnicity, performance status, pre-randomization disease response.

2.10 Participant Compliance

A consort diagram will be provided to illustrate study accrual and follow up. The enrolled participants who did not get to randomization, and those randomized but did not receive vaccination will be listed with reasons for non-adherence.

A table listing significant protocol deviations/violations will be provided by treatment group (if applicable). Compliance with protocol interventions will be evaluated as appropriate. Premature withdrawals will be described for each case.

In the tables/figures, the number of included participants will be provided/described for each analysis.

The metrics of manufacture products will be explored, and to be assessed with the treatment group association, and center effect. Exploratory results will be displayed with available data.

3. Analysis Plan

3.1 Analysis of the Primary Endpoint

Participant's disease status will be evaluated based on the International Uniform Response Criteria[4]. Before disease progression, all disease classifications including stringent complete response (sCR), complete response (CR), very good partial remission (VGPR), partial response (PR), stable disease (SD) are relative to participant's disease status at study entry. If participant develops disease progression, the disease classifications are relative to participant's best response since time of study entry.

The primary endpoint for the study is the proportion of participants alive and in complete response (CR) or stringent complete response (sCR) at one year post transplant, corresponding to approximately 10 months post randomization. The primary analysis will utilize the primary analysis population. The proportion of CR or sCR at one year post transplant will be estimated using frequencies in each group and compared between the treatment groups using a two-sample Z statistic for comparing two proportions. This test

will use the pooled proportion for the variance calculation under the null hypothesis, which is equivalent to the chi-squared test and has good asymptotic properties for the sample size and the expected proportions. A one-sided significance level of 0.10 will be used to assess whether the vaccine appears promising relative to control.

A secondary analysis stratified on disease response prior to randomization will be conducted using a Cochran-Mantel-Haenszel test, and a stratified odds ratio along with 80% confidence intervals will be estimated.

A secondary pairwise analysis of CR rates comparing the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm will also be conducted.

3.2 Analysis of the Secondary Endpoints

All secondary analyses will use a two-sided significance level of 5%.

3.2.1 Myeloma Response to Treatment

The disease response categories, including sCR, CR, VGPR, PR, SD, PD, will be tabulated at each assessment period. The proportion of participants alive and with sCR/CR/VGPR will be compared between the vaccine and the combined non-vaccine arms at 6 months, 1 year, and 2 years post-transplant using a chi-squared test.

A secondary pairwise analysis of response to treatment comparing the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm will also be conducted. Rates of conversion to CR will also be compared using a chi-square test among the subset of patients who are not in CR at the time of randomization.

3.2.2 Myeloma Progression

The event for this endpoint is defined as disease progression from CR/sCR or progressive disease for participants not in CR/sCR, or initiation of off protocol anti-myeloma therapy. The incidence of myeloma progression will be compared between the vaccine arm and the combined non-vaccine arms using Gray's test[5] and treating death (without documentation of disease progression) as a competing risk. Participants alive without disease progression at last observation will be censored at the date of last contact. A secondary pairwise analysis will be comparing the cumulative incidence of myeloma progression between the vaccine arm, lenalidomide/GM-CSF arm and lenalidomide alone arm.

3.2.3 Treatment-related Mortality (TRM)

The incidence of TRM will be compared between the vaccine arm and the combined non-vaccine arm, treating disease progression as a competing risk. An event is death from causes other than disease relapse or progression. Participants alive without disease progression at last contact will be censored. Gray's test will be used to compare the vaccine arm and the combined non-vaccine arms. A secondary pairwise analysis will be comparing the cumulative incidence of TRM between the vaccine arm, lenalidomide/GM-CSF arm and lenalidomide alone arm.

3.2.4 Progression-free Survival (PFS)

Death or disease progression will be considered as events for this endpoint. The time to event will be calculated as time from randomization to disease progression, death, initiation of non-protocol anti-myeloma therapy, loss to follow-up or the end of the study, whichever comes first. The Kaplan-Meier estimator will be constructed for each treatment arm. Progression-free survival will be compared between the vaccine and the combined non-vaccine arms using the log-rank test. The hazard ratios, along with confidence intervals, will be estimated from a Cox model with treatment group as a covariate.

A secondary analysis of PFS will be conducted to compare the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm in pairwise comparison.

3.2.5 Overall Survival (OS)

Death from any cause will be considered as an event for this endpoint. The time to event will be calculated as time from randomization to death, loss to follow-up or the end of the study, whichever comes first. Participants alive at the time of last observation will be censored at the date of last contact. The Kaplan-Meier estimator will be constructed for each treatment arm. Overall survival will be compared between the vaccine and the combined non-vaccine arms using the log-rank test. The hazard ratios, along with confidence intervals, will be estimated from a Cox model with treatment group as a covariate.

A secondary analysis of OS will be conducted to compare the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm in pairwise comparison.

3.2.6 Incidence of Toxicities Grade ≥ 3 per CTCAE version 4.0

Frequencies of grade 3 or higher toxicities based on NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4 will be tabulated by grade for each treatment arm, by toxicity type and by maximum grade at each time interval as well as the cumulative over time. Toxicity frequencies of participants developing Grade ≥ 3 will be compared between the vaccine and the combined non-vaccine arms using the Chi-square test.

3.2.7 Incidence of Infection

Grade 2 and 3 infections, as defined by the BMT CTN Technical MOP, occurring after randomization will be reported. The number of infections and the number of patients experiencing infections will be tabulated by type of infection, severity, and time period after transplant. The cumulative incidence of infections post randomization, treating death as a competing risk, will be compared between the vaccine and the combined non-vaccine groups using the Gray's test.

A secondary pairwise analysis that compares incidence of infections between the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm will be conducted.

3.2.8 Minimal Residual Disease Assessment

The proportions of participants with MRD present (MRD+) will be tabulated at randomization and after the completion of Cycle 9 of maintenance and compared between the vaccine and the combined non-vaccine groups using the Chi-square test.

A secondary pairwise analysis that compares proportions of MRD+ between the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide along arm will be conducted.

Data on MRD assessments will be retrieved from external lab and this data will be included in the primary manuscript. MRD analysis will not be included in the topline analysis.

3.3 Analysis of the Immunologic Endpoints

All analyses on immunologic endpoints will use a two-sided significance level of 5%.

3.3.1 Primary immunologic endpoint: Myeloma reactive T-cells

Log transformations will be used to induce normality in quantitative measurements, and if still non-normal, then nonparametric tests will be used. The primary endpoint of log 10 peak change in tumor reactive T cells from baseline will be compared across the 3 groups using analysis of variance, and if significant then two-sample t-tests will be conducted for each pairwise comparison to determine which groups are different from one another.

A secondary analysis of peak change in tumor reactive T cells will be done by comparing the proportions of patients who experience >10-fold increase in IFNγ expression, using a chi-squared test. Myeloma reactive T-cell response profiles over time will be compared between the treatment groups using linear mixed models for repeated measures data. Peak immune response as well as most recent immune response will be compared between those in CR and those not in CR at each assessment, using a two-sample t-test, to assess the relationship between immune response and clinical response. Peak and most recent immune response will also be considered as time-dependent covariates in a Cox proportional hazards model to assess their impact on progression-free survival.

3.3.2 Secondary immunologic endpoints

Additional exploratory analyses will be conducted in a similar fashion to examine a number of secondary immunologic endpoints, including:

1) antigen specific reactivity by tetramer analysis,

2) quantification of T-cell subsets and PD-1 expressing lymphocytes by flow cytometry

3) quantification of NK cell populations with inhibitor and activating markers,

4) NK-cell cytotoxic function as measured by IFNγ and CD107a degranulation in response to ex vivo exposure to autologous MM cells,

5) humoral response against autologous MM cells and myeloma associated antigens such as MUC1, and vaccine-induced myeloma-specific plasmablast responses.

In each case, log transformations will be considered to induce normality, and if still non-normal then nonparametric tests will be used. Profiles of these secondary immunologic

endpoints will be described at each time point for each group using summary statistics and compared between the groups using mixed models for repeated measures data. The correlation between the immune environment measures and the myeloma specific T-cell response will NOT be assessed. Instead, the correlation between the immune environment measures and the primary clinical outcome will be assessed and reported as exploratory analyses for the pooled treatment groups.

4. Template of Proposed Table/Figure/Listing (TFL) Shells

Table/Figure/Listing titles and layout are for illustration purposes only, and may not be the final layout or wording chosen for publications or presentations. Actual format of the tables and figures may differ and will be subject to change in the final analysis report and/or publication. See Appendix of this SAP for the exhibits title and shell.

5. References

[1] Rosenblatt, J. et al. Vaccination with dendritic cell/tumor fusions following autologous stem cell transplant induces immunologic and clinical responses in multiple myeloma patients. Clin Cancer Res 19, 3640-3648, doi:10.1158/1078-0432.CCR-13-0282 (2013).

[2] Luptakova, K. et al. Lenalidomide enhances anti-myeloma cellular immunity. Cancer Immunol Immunother 62, 39-49, doi:10.1007/s00262-012-1308-3 (2013).

[3] BGM Durie et al. International uniform response criteria for multiple myeloma. Leukemia (2006) 1-7.

[4] Jennison C, Turnbull BW. Group sequential methods with applications to clinical trials. Chapman and Hall/CRC, Boca Raton, 2000.

[5] Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Annals of Statistics 1988, 16: 1141-1154.

Appendix

EXHIBIT 1401-1: Participant Disposition and Follow-Up

A consort diagram will be provided showing the number of participants enrolled to the study, dropped out, received transplant, randomized to the study treatment, and treatment compliance as applicable. A table will be provided with descriptive statistics on length of follow-up by assigned treatment arm.

EXHIBIT 1401-2: Participant Demographics and Baseline Characteristics

Baseline characteristics and demographics will be described by frequencies and percentages for categorical covariates, and minimum, maximum, median, mean, and standard error for continuous covariates. The following covariates may be included:

- Treatment group assignment
- Strata (Risk status at time of randomization or other stratification factors)
- Gender
- Ethnicity
- Race
- Participant age
- Karnofsky performance score
- Disease response

Demographics for participants that did not make it to the randomization will also be described/summarized.

	Treatment Arm			
	Vaccine/GM-CSF/Lenalidomide (N=) N (%)	**Lenalidomide/GM-CSF (N=) N (%)**	**Lenalidomide alone (N=) N (%)**	**Total (N=) N (%)**
Gender				
Female				
Male				
Ethnicity				
Hispanic or Latino				
Not Hispanic or Latino				
Unknown				
Not Answered				
Race				
American Indian/Alaskan Native				
Asian				
Hawaiian/Pacific Islander				
Black or African American				
White				
More than One Race				
Other, Specify				
Unknown				
Not Answered				
Age, years				
Mean (SD)				
Median (Range)				
Karnofsky Performance Score				
100				

	Treatment Arm			
	Vaccine/GM-CSF/Lenalidomide (N=) N (%)	**Lenalidomide/GM-CSF (N=) N (%)**	**Lenalidomide alone (N=) N (%)**	**Total (N=) N (%)**
90				
80				
70				
Disease Response at Randomization				
Stringent Complete Response				
Complete Response				
Very Good Partial Response				
Partial Response				
Stable Response				

Time from enrollment to transplant and from transplant to randomization will be summarized in basic statistics including mean, standard deviation, range.

EXHIBIT 1401-3: Complete Response/Stringent Complete Response Rate at 1 Year Post Transplant

The primary endpoint is the proportion of patients alive and in CR or sCR at one year post transplant. The proportion of patients alive and in CR/sCR at 1 year post transplant will be described in the vaccine and no vaccine groups with 80% confidence intervals and compared between groups using a two-sample Z test comparing binomial proportions.

Proportion of Surviving Participants in CR/sCR at 1 Year Post Transplant

Alive and in CR/sCR	**Vaccine (N=) N (%)**	**Combined Non-vaccine (N=) N (%)**	**P-value**
YES	XX (XX.X%)	XX (XX.X%)	X.XXX
NO	XX (XX.X%)	XX (XX.X%)	
Alive and Not in CR/sCR	XX (XX.X%)	XX (XX.X%)	
Dead	XX (XX.X%)	XX (XX.X%)	
Not Evaluable[1]	XX	XX	

Note: [1] Participants that withdrew from the study or loss to follow up prior to the assessment time will be categorized into Not Evaluable.

A secondary analysis of CR/sCR rate stratified on disease response prior to randomization will be conducted and the stratified odds ratio will be estimated.

Stratum 1: sCR/CR at Randomization

Alive and in CR/sCR	**Vaccine (N=) N (%)**	**Combined Non-vaccine (N=) N (%)**	**P-value**
YES	XX (XX.X%)	XX (XX.X%)	X.XXX
NO	XX (XX.X%)	XX (XX.X%)	
Alive and Not in CR/sCR	XX (XX.X%)	XX (XX.X%)	
Dead	XX (XX.X%)	XX (XX.X%)	
Not Evaluable	XX	XX	

Stratum 2: VGPR/PR/SD at Randomization

Alive and in CR/sCR	**Vaccine (N=) N (%)**	**Combined Non-vaccine (N=) N (%)**	**P-value**
YES	XX (XX.X%)	XX (XX.X%)	X.XXX
NO	XX (XX.X%)	XX (XX.X%)	

Alive and Not in CR/sCR	XX (XX.X%)	XX (XX.X%)	
Dead	XX (XX.X%)	XX (XX.X%)	
Not Evaluable	XX	XX	

Cochran-Mantel-Haenszel Test for Stratification

Strata	Stratified Odds Ratio	80% Confidence Interval
Vaccine vs Combined Non-Vaccine	X.XX	X.XX, X.XX

*Note: P-value from heterogeneity test

A secondary pairwise analysis for CR/sCR rate will be conducted between vaccine and each non-vaccine group. Tabulation formats will be similar for each pair of group comparison.

Alive and in CR/sCR	**Vaccine (N=) N (%)**	**Non-vaccine Group 1: Lenalidomide/GM-CSF (N=) N (%)**	**P-value**
YES	XX (XX.X%)	XX (XX.X%)	X.XXX
NO	XX (XX.X%)	XX (XX.X%)	
Alive and Not in CR/sCR	XX (XX.X%)	XX (XX.X%)	
Dead	XX (XX.X%)	XX (XX.X%)	
Not Evaluable	XX	XX	

Alive and in CR/sCR	**Vaccine (N=) N (%)**	**Non-vaccine Group 2: Lenalidomide Alone (N=) N (%)**	**P-value**
YES	XX (XX.X%)	XX (XX.X%)	X.XXX
NO	XX (XX.X%)	XX (XX.X%)	
Alive and Not in CR/sCR	XX (XX.X%)	XX (XX.X%)	
Dead	XX (XX.X%)	XX (XX.X%)	
Not Evaluable	XX	XX	

EXHIBIT 1401-4: Disease Response

Disease response to treatment on surviving participants will be tabulated at each assessment time point post-transplant at 6 months, 1 year and 2 years.

Disease Response at Each Assessment Time Point Post Transplant

Assessment Time Point	Disease Response[1]	Vaccine (N=) N (%)	Lenalidomide/GM-CSF (N=) N (%)	Lenalidomide Alone (N=) N (%)	Total (N=) N (%)
6 months Post Transplant	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
1 Year Post Transplant	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
2 Years Post Transplant	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				

Proportion of Surviving Participants with sCR/CR/VGPR

Assessment Time Point Post Transplant	Vaccine (N=) N (%)	Combined Non-vaccine (N=) N (%)	P-value[2]
6 Months	XX (XX.X%)	XX (XX.X%)	X.XXX
1 Year	XX (XX.X%)	XX (XX.X%)	X.XXX
2 Years	XX (XX.X%)	XX (XX.X%)	X.XXX

Note:

[1] Participants that died or loss to follow up prior to the assessment time will be categorized as failures for this analysis.

[2] P-value from Chi-square test.

Disease response to treatment on surviving participants will be tabulated at each assessment time point during the maintenance therapy.

Assessment Time Point	Disease Response	Vaccine (N=) N (%)	Lenalidomide/GM-CSF (N=) N (%)	Lenalidomide Alone (N=) N (%)	Total (N=) N (%)
Cycle 3	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 6	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 9	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 12	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 15	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 18	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 21	Stringent Complete Response (sCR)				
	Complete Response (CR)				
	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				
Cycle 24	Stringent Complete Response (sCR)				
	Complete Response (CR)				

	Very Good Partial Response (VGPR)				
	Partial Response (PR)				
	Stable Disease (SD)				
	Progression (PD)				
	Death				
	Loss to Follow Up				

A secondary pairwise analysis for sCR/CR/VGPR rate will be conducted between vaccine and each non-vaccine group.

Assessment Time Point Post Transplant	**Vaccine (N=) N (%)**	**Lenalidomide/GM-CSF (N=) N (%)**	**Lenalidomide Alone (N=) N (%)**
6 Months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 Year	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 Years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Treatment Group Comparison	**p-value[1]**
Vaccine vs Lenalidomide/GM-CSF	0.XX
Vaccine vs Lenalidomide Alone	0.XX
Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

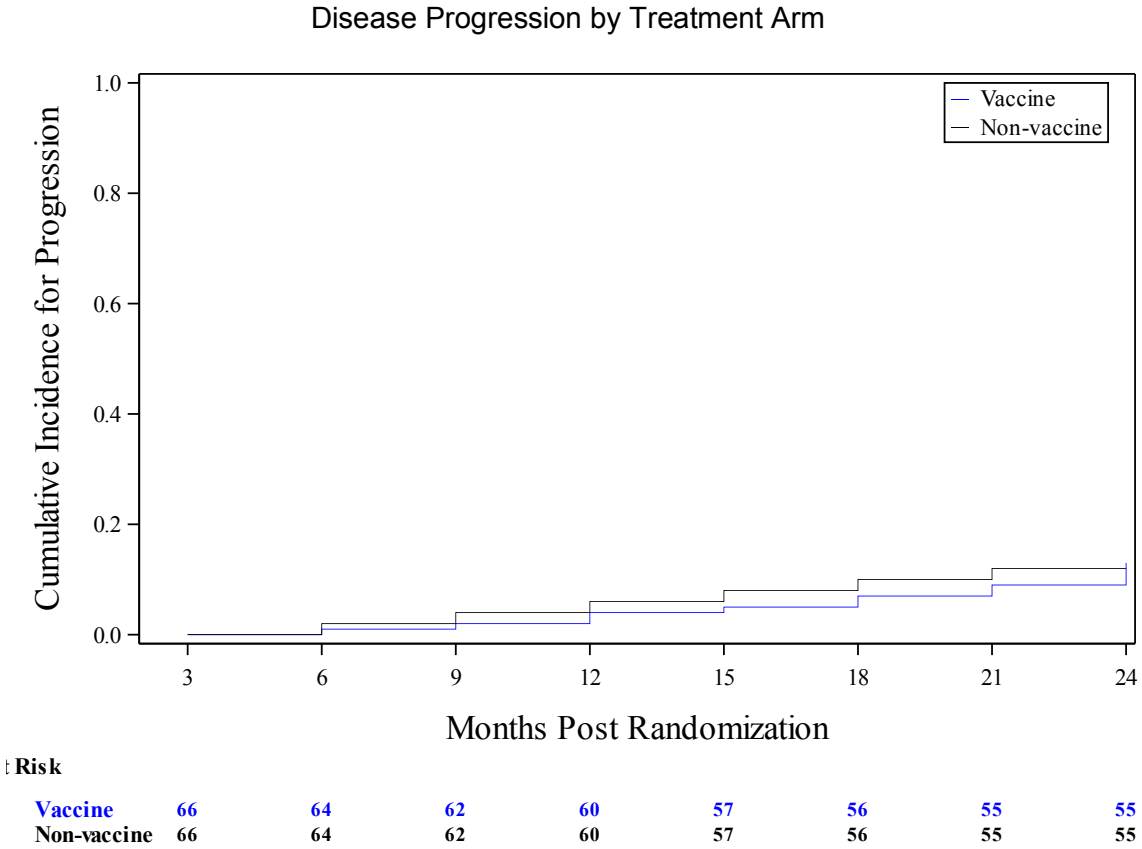
Note: [1] P-value from Chi-square test. The two-sided significance level is 0.05 for each pairwise comparison.

The proportions of participants achieving CR among the subset of participants who are not in CR at the time of randomization will be compared between groups.

CR/sCR Rate Among Non-CR at Randomization	**Vaccine (N=) N (%)**	**Lenalidomide/GM-CSF (N=) N (%)**	**Lenalidomide Alone (N=) N (%)**
6 Months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 Year	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 Years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

EXHIBIT 1401-5: Cumulative Incidence of Relapse/Progression

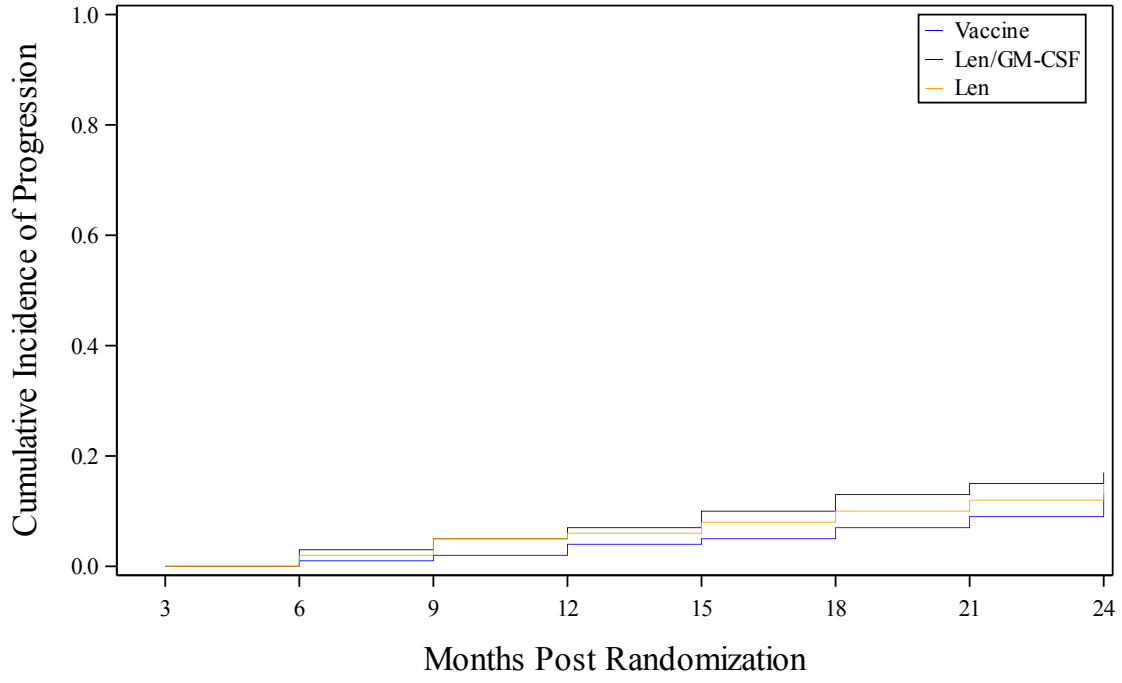
The cumulative incidence of myeloma progression/disease progression will be plotted.



Cumulative Incidence Estimates and 95% Confidence Intervals for Disease Progression:

Disease Progression	Vaccine (N=)	Combined Non-Vaccine (N=)	P-value from Gray's Test
At 1 Year (95% CI)			
At 2 Years (95% CI)			

For the secondary pairwise analysis, the cumulative incidence of myeloma progression/disease progression will be plotted by each treatment group.



Risk

Vaccine	66	64	62	60	57	56	55	55
Len/GM-CSF	33	32	32	31	31	30	29	29
Len	33	31	30	30	29	28	27	27

Cumulative Incidence Estimates and 95% Confidence Intervals for Disease Progression:

Disease Progression	Vaccine (N=)	Lenalidomide/GM-CSF (N=)	Lenalidomide Alone (N=)
At 1 Year (95% CI)			
At 2 Years (95% CI)			

Gray's Test for Pairwise Comparisons Post Randomization

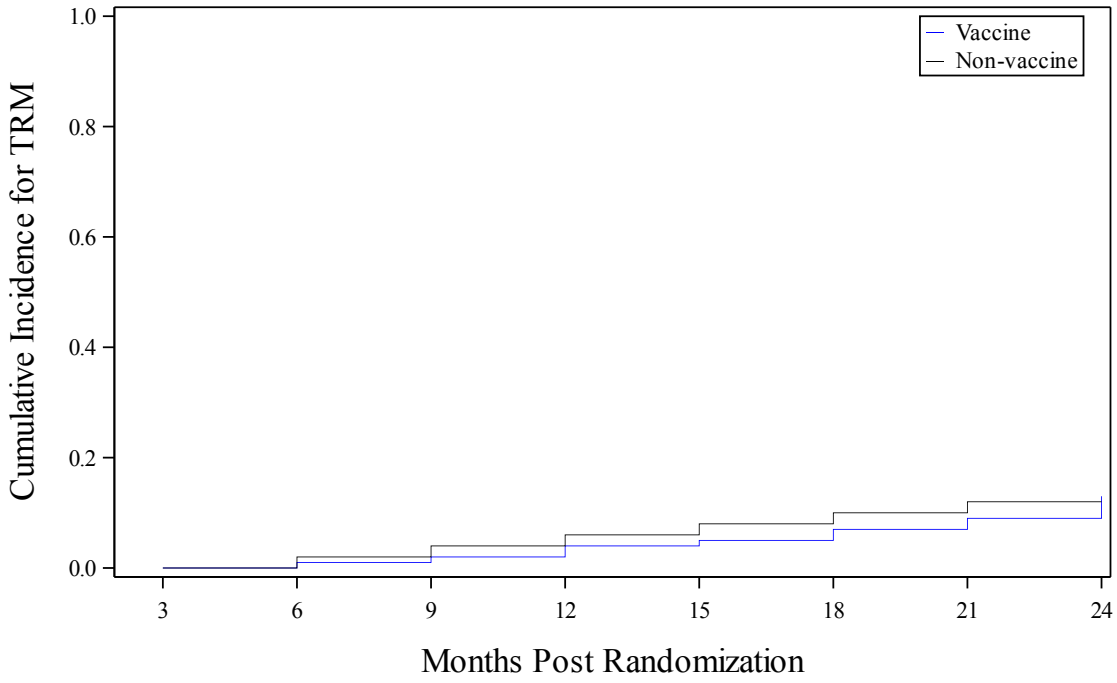
Treatment Group Comparison	p-value[1]
Vaccine vs Lenalidomide/GM-CSF	0.XX
Vaccine vs Lenalidomide Alone	0.XX
Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

Note: [1]The two-sided significance level is 0.05 for each pairwise comparison.

EXHIBIT 1401-6: Cumulative Incidence of Treatment-related Mortality (TRM)

The cumulative incidence of treatment-related mortality will be plotted.

Treatment-related Mortality by Treatment Arm



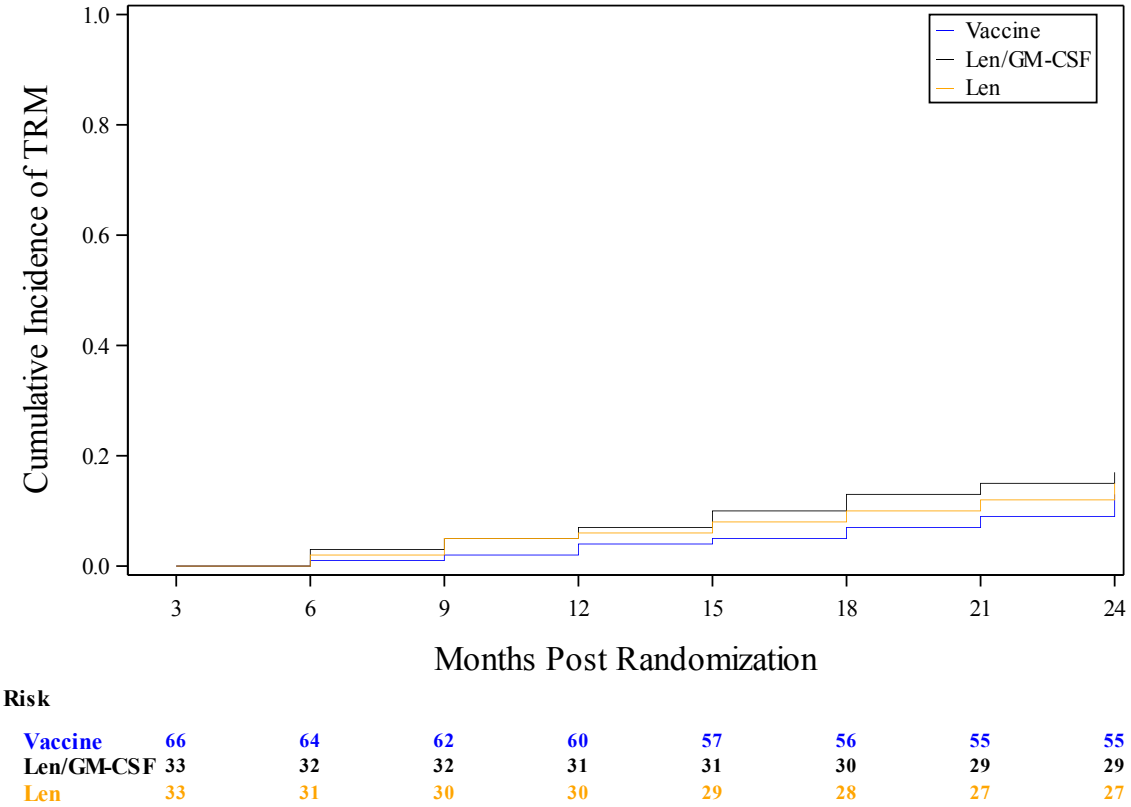
t Risk

Vaccine	66	64	62	60	57	56	55	55
Non-vaccine	66	64	62	60	57	56	55	55

Cumulative Incidence Estimates and 95% Confidence Intervals for TRM:

TRM	Vaccine (N=)	Combined Non-Vaccine (N=)	P-value from Gray's Test
At 1 Year (95% CI)			
At 2 Years (95% CI)			

For the secondary pairwise analysis, the cumulative incidence of treatment-related mortality will be plotted by three treatment groups.



Risk

Vaccine	66	64	62	60	57	56	55	55
Len/GM-CSF	33	32	32	31	31	30	29	29
Len	33	31	30	30	29	28	27	27

Cumulative Incidence Estimates and 95% Confidence Intervals for TRM:

TRM	Vaccine (N=)	Lenalidomide/GM-CSF (N=)	Lenalidomide Alone (N=)
At 1 Year (95% CI)			
At 2 Years (95% CI)			

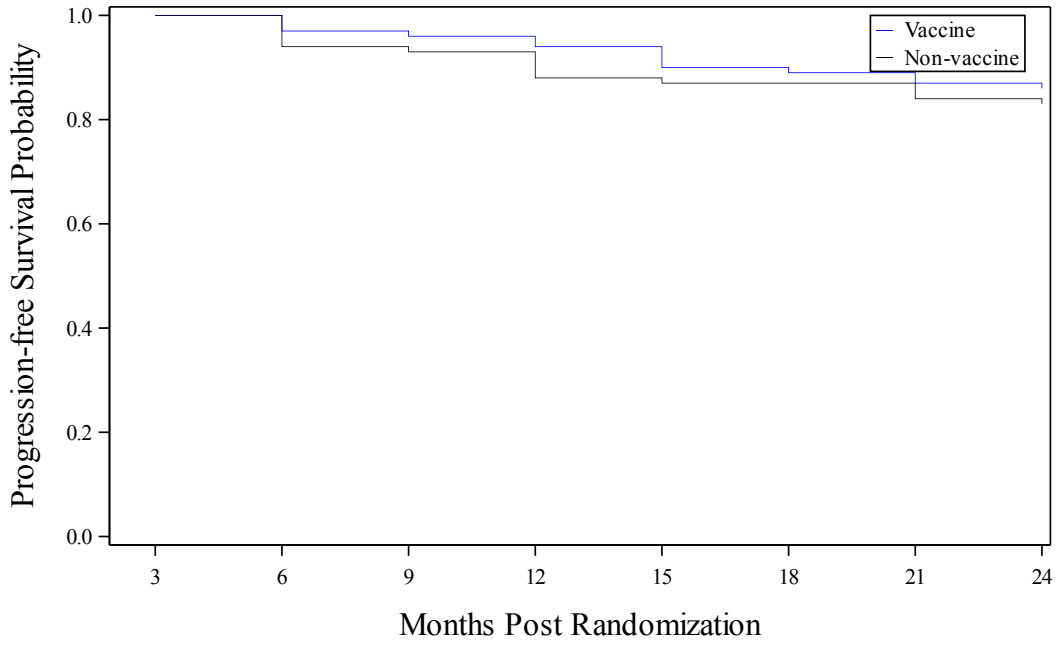
Gray's Test for Pairwise Comparisons

Treatment Group Comparison	p-value[1]
Vaccine vs Lenalidomide/GM-CSF	0.XX
Vaccine vs Lenalidomide Alone	0.XX
Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

Note: [1]The two sided-significance level is 0.05 for each pairwise comparison.

EXHIBIT 1401-7: Progression-Free Survival (PFS)

The progression-free survival post randomization will be plotted and summarized



Risk

Vaccine	66	64	62	60	57	56	55	55
Non-vaccine	66	62	61	56	56	56	54	53

*Note: P-value from log-rank test can be added to the plot

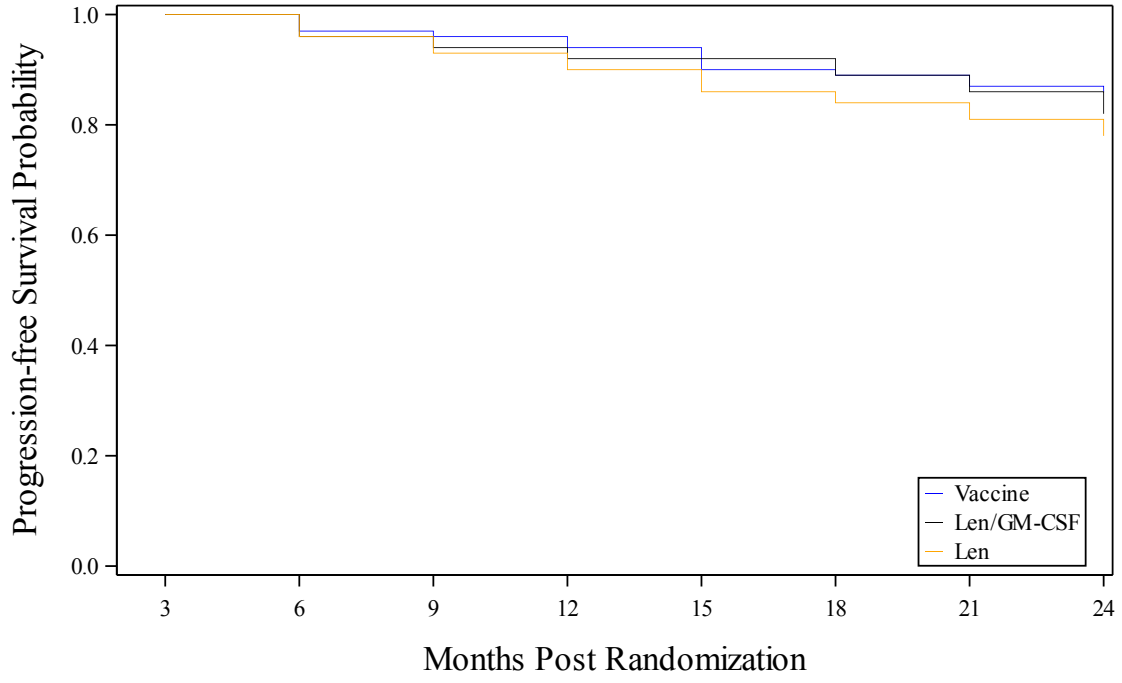
Kaplan Meier Estimates and 95% Confidence Intervals for PFS

Progression-free Survival	Vaccine (N=)	Non-Vaccine (N=)	P-value from Log-rank test
At 1 Year (95% CI)			
At 2 Years (95% CI)			

Cox Proportional Hazards Regression Model for PFS

Covariates	Level	N	HR	95% CI	P-value
Treatment Group	Non-vaccine	XX	1.00		
	Vaccine	XX	X.XX	X.XX – X.XX	X.XX

For the secondary pairwise analysis, the progression-free survival will be plotted by three treatment groups.



Risk

Vaccine	66	64	62	60	57	56	55	55
Len/GM-CSF	33	32	32	31	31	30	29	29
Len	33	31	30	30	29	28	27	27

Kaplan Meier Estimates and 95% Confidence Intervals for PFS:

Progression-free Survival	Vaccine (N=)	Lenalidomide/GM-CSF (N=)	Lenalidomide Alone (N=)
At 1 Year (95% CI)			
At 2 Years (95% CI)			

Log Rank Test for Pairwise Comparisons

Treatment Group Comparison	p-value[1]
Vaccine vs Lenalidomide/GM-CSF	0.XX
Vaccine vs Lenalidomide Alone	0.XX
Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

Note: [1]The two-sided significance level is 0.05 for each pairwise comparison.

EXHIBIT 1401-8: Overall Survival (OS)

The overall survival post randomization will be plotted and summarized.

The summary table and figures will follow exactly the same format as for PFS in Exhibit 1401-7.

EXHIBIT 1401-9: Incidence of Toxicities Grade ≥ 3 per CTCAE Version 4.0

Toxicities will be summarized in system organ class (SOC). If investigators have interest in specific toxicities with high incidence, we can tabulate frequencies for these toxicities per request. Toxicity frequencies by SOC and breakdown down by grade 3, grade 4, grade 5 can be summarized at each assessment time point.

Category (SOC)	Involved Toxicity/Organ
Auditory Disorders	hearing loss
Blood and Lymphatic Disorders	anemia, lymphopenia, neutropenia, thrombocytopenia, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, febrile neutropenia
Cardiovascular Disorders	left ventricular systolic dysfunction, cardiac arrhythmia, myocardial infarction, pericardial effusion, new or worsening heart failure, pericarditis
Endocrine Disorders	hyperthyroidism, hypothyroidism
GI Disorders	abdominal pain, anorexia, constipation, diarrhea, dry mouth, dyspepsia, nausea, oral mucositis, vomiting
General Disorders	non-cardiac chest pain, chills, generalized edema, fatigue, fever
Hemorrhagic Disorders	hemorrhage
Hepatobiliary/Pancreas Disorders	hepatitis, liver failure, pancreatitis, bilirubin, ALT, AST, alkaline phosphatase
Immune System Disorders	allergic reaction, anaphylaxis
Investigations	increased creatinine, weight loss, prolongation of QTc interval
Metabolism and Nutrition Disorders	dehydration, hypercalcemia, hyperglycemia, hypoglycemia, hypokalemia, hyponatremia, tumor lysis syndrome
Musculoskeletal and Connective Tissue Disorders	arthralgia, myalgia, muscle weakness, musculoskeletal pain
Nervous System Disorders	anxiety, ataxia, confusion, depression, dizziness, headache, insomnia, somnolence, seizure, stroke, tremor, cranial palsy, depressed level of consciousness, edema cerebral, encephalopathy, neuralgia, neuropathy, PRES, spinal cord compression (non-malignant), syncope
Ocular/Visual Disorders	conjunctivitis, blurred vision
Renal Disorders	cystitis noninfective, acute kidney injury, chronic kidney disease
Respiratory, Thoracic and Mediastinal Disorders	cough, dyspnea, hypoxia, sinusitis, sore throat, adult respiratory distress syndrome, pleural effusion (non-malignant), pneumonitis, pulmonary hypertension
Skin and Subcutaneous Tissue Disorders	dry skin, pruritus, rash, erythema multiforme, pyoderma gangrenosum, Sweet's syndrome (acute neutrophilic dermatosis)
Vascular Disorders	lymphedema, hypertension, hypotension, capillary leak syndrome, thromboembolic event, vasculitis
Abnormal Liver Symptoms	jaundice, hepatomegaly, right upper quadrant pain, weight gain (>5%) from baseline

Toxicity Summary by System Organ Class

	Grade 3-5 Toxicities					
	Vaccine (N=)		Lenalidomide/GM-CSF (N=)		Lenalidomide Alone (N=)	
System Organ Class	**# Event**	**# Participants[1]**	**# Event**	**# Participants[1]**	**# Event**	**# Participants[1]**
Auditory Disorders						
Blood and Lymphatic System Disorders						
Cardiac disorders						
Endocrine Disorders						
Gastrointestinal Disorders						
General Disorders						
Hemorrhagic Disorders						
Hepatobiliary/Pancreas Disorders						
Immune System Disorders						
Investigations						
Metabolism and Nutrition Disorders						
Musculoskeletal and Connective Tissue Disorders						
Nervous System Disorders						
Ocular/Visual Disorders						
Renal and Urinary Disorders						
Respiratory,Thoracic,and Mediastinal Disorders						
Skin and Subcutaneous Tissue Disorders						
Vascular Disorders						
Total						

Toxicity Summary by Time Period

Assessment Time Period	**Vaccine**				**Lenalidomide/GM-CSF**				**Lenalidomide Alone**			
	# Pts[1]	**# Pts with an event reported**	**# Events**	**% Pts with events**	**# Pts[1]**	**# Pts with an event reported**	**# Events**	**% Pts with events**	**# Pts[1]**	**# Pts with an event reported**	**# Events**	**% Pts with events**
Within Day 100												
100 Days to 1 Year												
1 Year to 2 Years												
Overall												

EXHIBIT 1401-10: Incidence of Infections

Infection events will be tabulated for two periods.
Period 1: From transplant to Randomization:

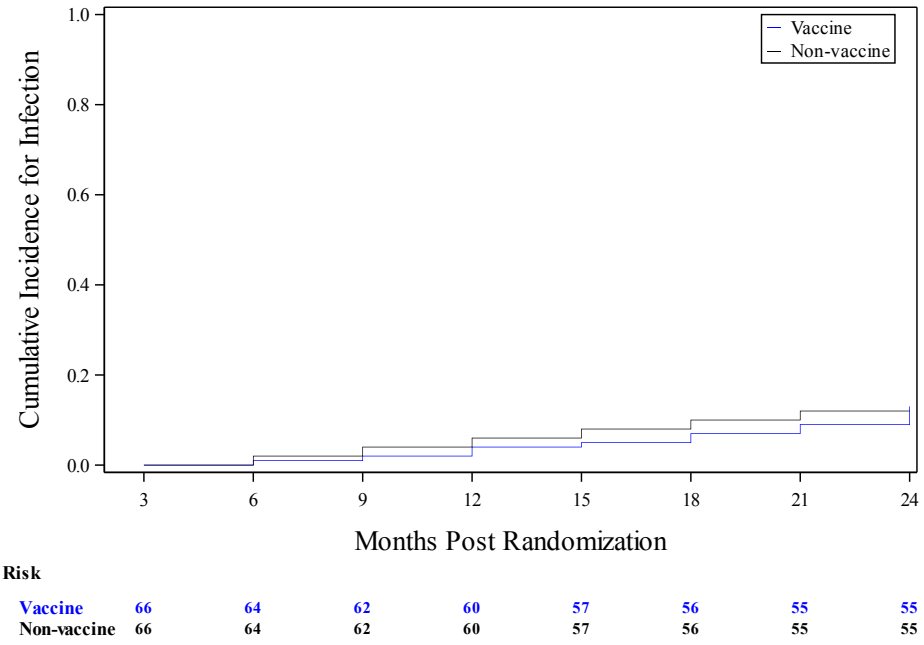
	Total
	N %
# Participants transplanted	
# Participants with Infections	
# Participants with Infection Reports =1 =2 =3 =4 =5 >=6	
Total Infection Events	
Infection Period Within First month of Transplant Post first month of Transplant	
Maximum Severity by Participant None Grade 2 Grade 3	
Infection by Type (# of Participants) Bacterial Viral Fungal Protozoal Other	

Period 2: Post randomization by treatment arm

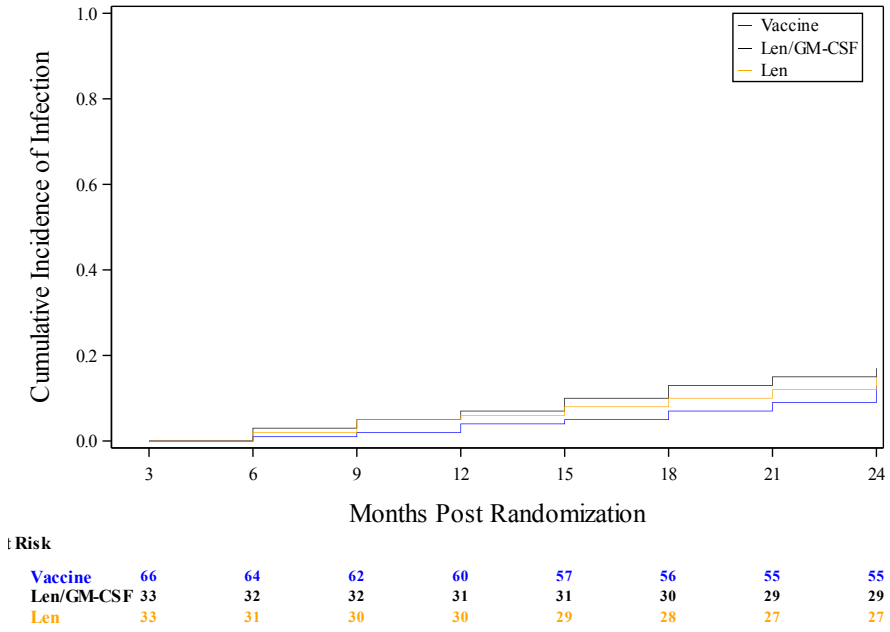
	Treatment Arm			
	Vaccine	Lenalidomide/GM-CSF	Lenalidomide Alone	Total
	N %	N %	N %	N %
# Participants Randomized				
# Participants with Infections				
# Participants with Infection Reports =1 =2 =3 =4				

	Treatment Arm			
	Vaccine	Lenalidomide/GM-CSF	Lenalidomide Alone	Total
	N %	N %	N %	N %
=5				
>=6				
Total Infection Events				
Infection Period				
First 100 Days				
100 Days to 1 Year				
1 Year to 2 Years				
Maximum Severity by Participant				
None				
Grade 2				
Grade 3				
Infection by Type (# of Participants)				
Bacterial				
Viral				
Fungal				
Protozoal				
Other				

The cumulative incidence of Grade 3 infections will be compared between the vaccine and the combined non-vaccine groups.



For the secondary pairwise analysis, the cumulative incidence will be plotted by three treatment groups.



Cumulative Incidence Estimates and 95% Confidence Intervals for Grade 3 Infections

Incidence of Grade 3 Infections	Vaccine (N=)	Lenalidomide/GM-CSF (N=)	Lenalidomide Alone (N=)
At 1 Year (95% CI)			
At 2 Years (95% CI)			

Log Rank Test for Pairwise Comparisons

Treatment Group Comparison	P-value[1]
Vaccine vs Lenalidomide/GM-CSF	0.XX
Vaccine vs Lenalidomide Alone	0.XX
Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

Note: [1]The two-sided significance level is 0.05 for each pairwise comparison.

EXHIBIT 1401-11: Minimal Residual Disease Assessment

The proportions of patients with MRD present (MRD+) will be described using frequencies at pre-randomization and 9th cycle post randomization and compared between the vaccine arm with the no-vaccine arms combined using the chi-square test.

MRD by Treatment Group

% MRD +	Vaccine (N=)	Non-vaccine (N=)	P-value
Pre-randomization			—
Post-randomization at Cycle 9			

A secondary pairwise analysis of MRD comparing the vaccine arm, lenalidomide/GM-CSF arm and the lenalidomide alone arm will also be conducted.

% MRD +	Vaccine (N=)	Lenalidomide/GM-CSF (N=)	Lenalidomide Alone (N=)	P-value
Pre-randomization				—
Post-randomization at Cycle 9				

Pairwise Comparisons

	Treatment Group Comparison	P-value
Post-randomization at Cycle 9	Vaccine vs Lenalidomide/GM-CSF	0.XX
	Vaccine vs Lenalidomide Alone	0.XX
	Lenalidomide/GM-CSF vs Lenalidomide Alone	0.XX

Note: [1]The two-sided significance level is 0.05 for each pairwise comparison.

EXHIBIT 1401-12: Primary Immunologic Endpoint: Myeloma Reactive T Cells

Myeloma-reactive T cells, as defined by the percentage of circulating CD4+ and CD8+ T cells that express IFNγ following ex vivo exposure to autologous tumor lysate will be assess in both treatment arms and summarized in below table. Log transformations will be used to induce normality in quantitative measurements, and if still non-normal, then nonparametric tests will be used. The primary endpoint of log 10 peak change in tumor reactive T cells from baseline will be compared across the 3 groups using analysis of variance (ANOVA), and if significant then two-sample t-tests will be conducted for each pairwise comparison to determine which groups are different from one another. If normal, two-sample t-test will be used for pairwise comparison. If not, the non-parametric Kruskal-Wallis and Wilcoxon tests will be used. The two-sided significance level 0.05 will be used for each comparison.

ANOVA for Log 10 Peak Change in Tumor Reactive T cells from Baseline

Analysis of Variance on primary immunologic endpoint	**P-value**
Log 10 Peak Change From Baseline	
Pairwise Comparison if above is significant	
Vaccine vs Lenalidomide/GM-CSF	
Vaccine vs Lenalidomide Alone	
Lenalidomide/GM-CSF vs Lenalidomide Alone	

Summary Statistics Table for Myeloma Reactive T Cells by Assessment Time Points

Endpoint	**Assessment Time Point**	**Vaccine**	**Lenalidomide/GM-CSF**	**Lenalidomide Alone**
% CD8+ and CD4+ that express IFNγ	Baseline			
	Cycle 1			
	Cycle 2			
	Cycle 3			
	Cycle 4			
	Cycle 9			
	Change from Baseline to Cycle 1			
	Change from Baseline to Cycle 2			
	Change from Baseline to Cycle 3			
	Change from Baseline to Cycle 4			
	Change from Baseline to Cycle 9			
	Peak change from Baseline			
% Participants with >2.4-fold increase in IFNγ expression				
% Participants with >10-fold increase in IFNγ expression				

Note: Descriptive Statistics including N, Mean (Std), Median (Range), percentage will be calculated for each treatment group

Secondary analyses of myeloma reactive T cell will be conducted and summarized.

Linear Mixed Model for Repeated Measurements

Treatment Group	Least Squares Means	Std Err	P-value
Vaccine			
Lenalidomide/GM-CSF			
Lenalidomide Alone			
Difference (Vaccine – Lenalidomide/GM-CSF)			
Difference (Vaccine – Lenalidomide Alone)			
Difference (Lenalidomide/GM-CSF – Lenalidomide Alone)			

Myeloma Reactive T Cells by Clinical Response (best clinical response)

Myeloma reactive T cells	Participants in CR/sCR	Participants not in CR/sCR	P-value
Baseline			
Change from Baseline to Cycle 1			
Change from Baseline to Cycle 2			
Change from Baseline to Cycle 3			
Change from Baseline to Cycle 4			
Change from Baseline to Cycle 9			
Peak Change from baseline Over Time			

Multivariate Cox Proportional Hazards Regression Model for PFS

Covariates	N	HR	Parameter Estimate	95% CI	P-value
Treatment group					
Non-vaccine	XX	1.000	-	-	-
Vaccine	XX	X.XXX		(X.XXX, X.XXX)	X.XXX
Peak % CD8+ and CD4+ that express IFNγ (as time-dependent covariate, treated as continuous variable)					
Treatment group					
Non-vaccine	XX	1.000	-	-	-
Vaccine	XX	X.XXX		(X.XXX, X.XXX)	X.XXX
Most Recent % CD8+ and CD4+ that express IFNγ (as time-dependent covariate, treated as continuous variable)					

EXHIBIT 1401-13: Secondary Immunologic Endpoints

Additional exploratory analyses will be conducted in a similar fashion to examine a number of secondary immunologic endpoints, including: 1) antigen specific reactivity by tetramer analysis, 2) quantification of T-cell subsets and PD-1 expressing lymphocytes by flow cytometry 3) quantification of NK cell populations with inhibitor and activating markers, 4) NK-cell cytotoxic function as measured by IFNγ and CD107a degranulation in response to ex vivo exposure to autologous MM cells, and 5) humoral response against autologous MM cells and myeloma associated antigens such as MUC1, and vaccine-induced myeloma-specific plasmablast responses.

Profiles of these secondary immunologic endpoints will be described at each time point for each group using summary statistics and compared between the groups using mixed models for repeated measures data, using the same format as described in Exhibit 1401-12. Exploratory analysis on the association of secondary immunologic endpoints and the primary clinical outcome ((1-year disease response) will be conducted for each secondary immunologic endpoint with treatment groups pooled.

Summary Statistics Table for Secondary Immunologic Endpoints by Treatment Group

Endpoint	Assessment Time Point	Vaccine	Lenalidomide/GM-CSF	Lenalidomide Alone
Myeloma Antigen-specific T Cells: CD8+ binding tetramer	Baseline			
	Cycle 1			
	Cycle 2			
	Cycle 3			
	Cycle 4			
	Cycle 9			
Functionla Characteristics of Tetramer + Population IFNγ, granzyme B, IL-4, IL-10	Baseline			
	Cycle 1			
	Cycle 2			
	Cycle 3			
	Cycle 4			
	Cycle 9			
Subset of T Cells: CR45RA, CR45RO, CD27, CD62L, CD4/CD25/FOP3, CD11b, HLA-dr, CD14, CD15, CD33	Baseline			
	Cycle 1			
	Cycle 2			
	Cycle 3			
	Cycle 4			
	Cycle 9			
NK Cells	Prior to Cycle 1			
	Cycle 2+7 days			

	Cycle 3			
	Cycle 4+7days			
	Cycle 9			
Vaccine-induced myeloma-specific Plasmabast Response	Baseline			
	Cycle 2			
	Cycle 2+7 days			
	Cycle 4			

Note: Descriptive Statistics including N, Mean (Std), Median (Range) will be calculated for each treatment group

e.g. for the CD8+ endpoint,

Linear Mixed Model for Repeated Measurements

CD8+ by Treatment Group	Least Squares Means	Std Err	P-value
Vaccine			
Lenalidomide/GM-CSF			
Lenalidomide Alone			

Secondary Immunologic Endpoint CD8+ by Primary Clinical Endpoint

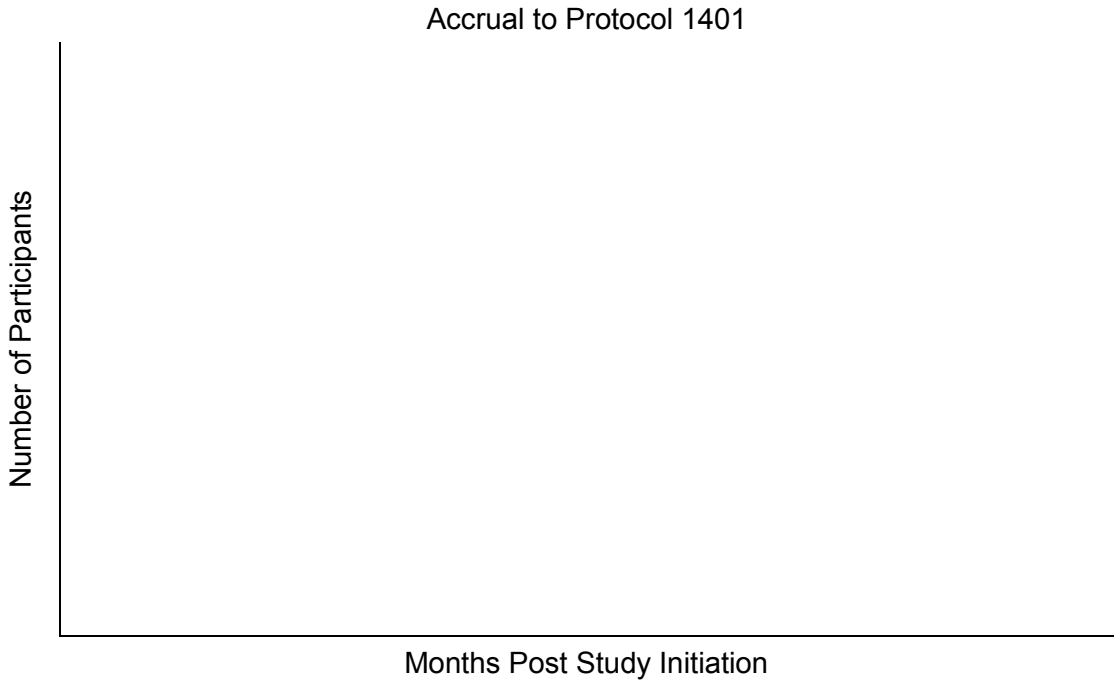
Myeloma Antigen-specific T Cells: CD8+ binding tetramer	Participants in CR/sCR @ 1 year	Participants not in CR/sCR @ 1 year	P-value
Baseline			
Change from Baseline to Cycle 1			
Change from Baseline to Cycle 2			
Change from Baseline to Cycle 3			
Change from Baseline to Cycle 4			
Change from Baseline to Cycle 9			
Peak Change from baseline Over Time			

If normal, two-sample t-test will be used for the comparison. If not, non-parametric test will be used.

Supplemental Exhibit 1401-1: Enrollment

A table will be provided showing actual monthly accrual for each participating center from study initiation to accrual closure. The number of randomized participants will be provided in a separate table.

A figure will be provided showing projected and actual accrual from study initiation to accrual closure.



Supplemental Exhibit 1401-2: Significant Protocol Deviations

A listing of significant protocol deviations will be provided to describe each deviation.

Supplemental Exhibit 1401-3: Primary Cause of Death

A table summarizing the primary cause of death by treatment group will be provided.

Supplemental Exhibit 1401-4: Adverse Events

A table summarizing the MedDRA-coded System Organ Class (SOC) of the adverse events reported will be provided by treatment group.

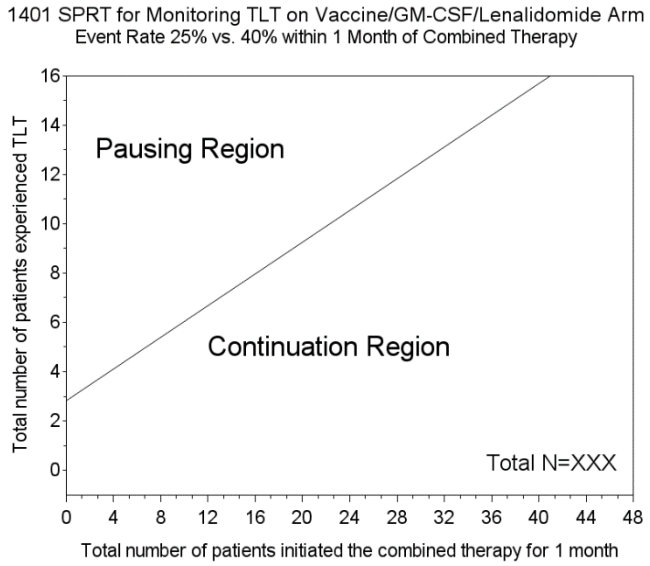
Supplemental Exhibit 1401-5: Serious or Grades 3-5 Adverse Events

A table summarizing the SOC of the serious or Grades 3-5 adverse events will be provided by treatment group.

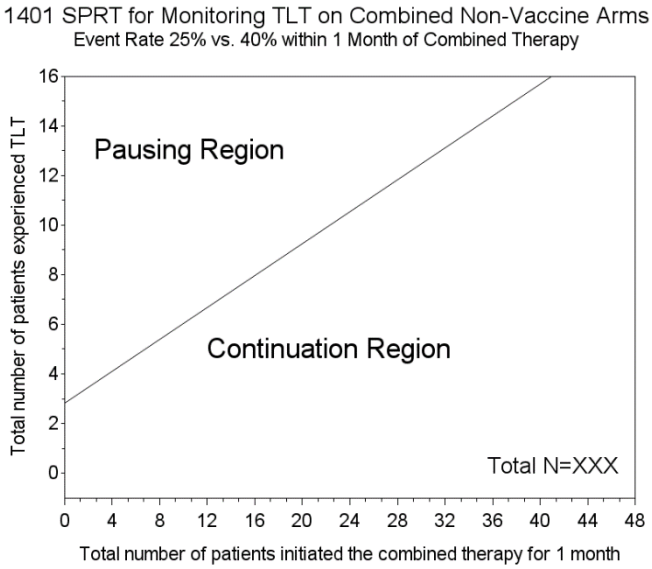
	Grade 3-5 AEs Post-Randomization							
	Vaccine (N=)		Lenalidomide/GM-CSF (N=)		Lenalidomide Alone (N=)		Total	
System Organ Class	# Event	# Participants	# Event	# Participants	# Event	# Participants	# Event	# Participants
Auditory Disorders								
Blood and Lymphatic System Disorders								
Cardiac disorders								
Endocrine Disorders								
Gastrointestinal Disorders								
General Disorders								
Hemorrhagic Disorders								
Hepatobiliary/Pancreas Disorders								
Immune System Disorders								
Investigations								
Metabolism and Nutrition Disorders								
Musculoskeletal and Connective Tissue Disorders								
Nervous System Disorders								
Ocular/Visual Disorders								
Renal and Urinary Disorders								
Respiratory,Thoracic,and Mediastinal Disorders								
Skin and Subcutaneous Tissue Disorders								
Vascular Disorders								
Total								

Supplemental Exhibit 1401-6: Safety Monitoring (Safety Endpoints)

Figure of SPRT to illustrate safety monitoring stopping guidelines.



Note:
N = The total number of patients randomized to the treatment arm and initiated the combined therapy.
TLT = Treatment Limiting Toxicity.



Note:
N = The total number of patients randomized to the treatment arm and initiated the combined therapy.
TLT = Treatment Limiting Toxicity.