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The GlaxoSmithKline group of companies 208470

Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for Open-Label Pilot Study to Assess the Safety, Tolerability and Antitumor Activity of Genetically Engineered NY-ESO-1 Specific (c259) T-cells Alone or in Combination with Pembrolizumab in HLA-A2+ Subjects with NY-ESO-1 and/or LAGE-1a Positive Relapsed and Refractory Multiple Myeloma
Compound Number	:	GSK3377794
Effective Date	:	23-APR-2021

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the abbreviated Clinical Study Report for Protocol 208470.
- This RAP is intended to describe the planned safety, tolerability and efficacy analyses required for the study.
- This RAP will be provided to study team members to convey the planned content of the Statistical Analysis Complete (SAC) deliverable.

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TABLE OF CONTENTS

PAGE

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 208470:

Protocol Revision Chronology:		
Version 01	19-Dec-2016	Original
Version 02 (Amendment 1)	13-Mar-2017	Changes included: - Integration of the sequential screening tests for HLA-genotyping and NY-ESO-1/LAGE-1a antigen expression level determination by RT-PCR. - Update to Pembrolizumab background. - Miscellaneous minor corrections/clarifications.
Version 03 (Amendment 2)	24-Jul-2018	Subsequent to the licensing of Adaptimmune product NY-ESO by GlaxoSmithKline (GSK), the purpose of this protocol amendment was to: - Delete or replace references to Adaptimmune or its staff with that of GSK and its authorized agents to align with the change of sponsorship. - Make administrative changes to align with GSK processes and procedures. - Make changes to lymphodepletion regimen.
Version 04 (Amendment 3)	17-Oct-2018	Changes made to the protocol were requested by the FDA as a result of safety events which included 2 reports of Guillain-Barré Syndrome in subjects who received chemotherapy and GSK3377794 during clinical trials.
Version 05 (Amendment 4)	19-Sep-2019	Several changes were made related to FDA requests, including updating Inclusion Criterion #5, adding study stopping rules, and updating Encephalopathy (now Immune Effector Cell-Associated Neurotoxicity or ICANS) and CRS grading and management criteria based upon American Society for Transplantation and Cellular Therapy, Lee, 2019 guidance. Also, changes were made to the lymphodepletion regimen for older subjects, and the randomization scheme was removed to first enrol subjects into Arm 1 (NY-ESO-1c259 T single infusion).
Version 06 (Amendment 5)	24-Feb-2020	This amendment restructured the protocol for a clearer presentation of the 3-part study design. The amendment also introduced the intent to enrol, treat, and monitor for safety and efficacy subjects who have previously received a BCMA-targeted therapy as a separate line of therapy potentially in a separate clinical trial. Additionally, several

Protocol Revision Chronology:		
		eligibility criteria were updated, clarification was made that enrolment into Arm 2 only (versus both arms) would be paused following start of lymphodepletion of the third subject, and the version of International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma used in efficacy determination was updated from 2011 to 2016.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Change to Protocol Specified Statistical Analysis Plan

In this RAP, there are no changes or deviations to the statistical analysis from that described in the latest amended protocol (dated 24-Feb-2020) other than the following:

- Definitions of analysis populations, removing the As-Treated Population.
- Explicit instruction to summarize data for the Modified Intent-to-Treat (mITT) Population (instead of Intent-to-Treat [ITT] Population), when the two populations are identical.
- Efficacy endpoints described in the Efficacy Analyses section (Section 7) as Primary and Secondary Efficacy Endpoints, rather than overall Secondary Endpoints.
- Protocol Section 11.2 states that *"Interim analyses to inform internal decision making may be performed for each arm after enrolment to the arm is complete and all enrolled subjects in that arm who will receive NY-ESO-1^{c259}T have done so and of those: all have completed at least three disease assessments since infusion or have progressed (And if progressed prior to the Week 9 visit have been followed up for safety for a minimum of 9 weeks following T-cell infusion) or have died or were withdrawn from the study."* As accrual to the study was halted prior to completing enrolment in either arm, the interim analysis was not conducted. Thus, references to the interim analysis and the evaluable population have been removed from the RAP.
- Protocol Section 3.1.3 and Section 4.3 state that "*A subject will be considered to have completed the treatment phase of the study when he/she has progression of disease or 108 weeks after NYESO-1^{c259}T-cell infusion, whichever is sooner".* In this RAP, death is also considered a criterion for completion of the treatment phase.
- Protocol Section 4.4 states that "*This study will be considered complete when the last subject has been rolled over into the LTFU protocol."* This RAP notes that study completion can also occur in the case that one or more patients have withdrawn from the parent study (including lost to follow-up), completed long-term follow-up in this study, or expired prior to rolling over into the LTFU protocol.
- Protocol Section 6.1 states that *"Subjects receiving any of palliative radiation therapy that could be foreseen impacting disease course or disease assessments will be censored for the purposes of determining PFS."* In this RAP, new anti-cancer therapy that would result in censoring PFS only includes systemic therapy.
- This study was terminated early; thus, only analyses relevant to these limited data are presented.
- Due to early termination of the study, only a final analysis will be performed. Thus, a primary analysis has been removed from Section 3.
- According to GSK standards, Listing of Race (DM9) is required per ICH E3. Due to differences in Adaptimmune data collection, only Listing of Demographic Characteristics (DM2) will be displayed which will include race information.

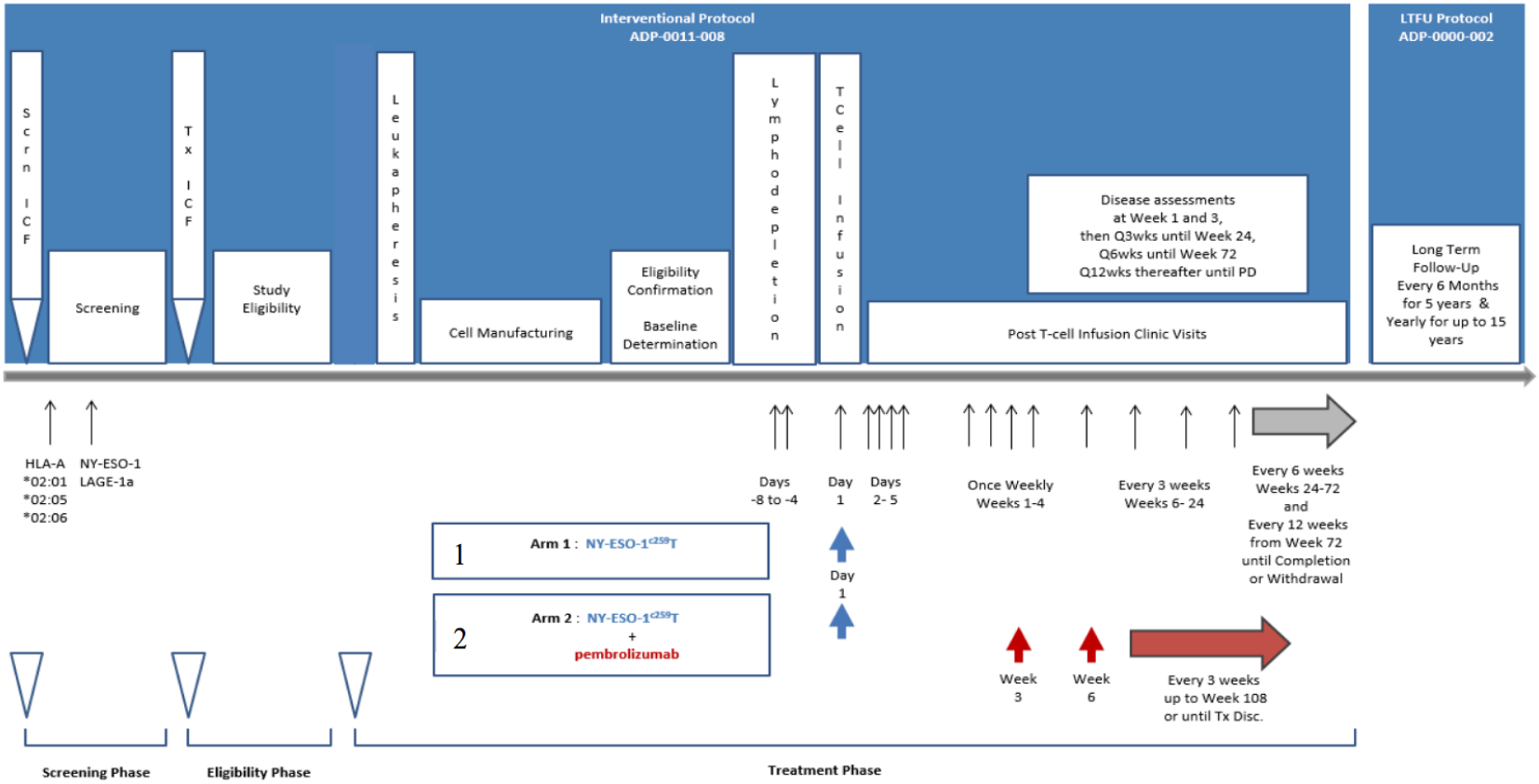
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To describe the safety and tolerability of autologous genetically modified T-cells (NY-ESO-1c259T) alone (Arm 1) or in combination with pembrolizumab (Arm 2) in participants who are human leukocyte antigen HLA-A*02:01, HLA-A*02:05, and/or HLA-A*02:06 positive and have NY-ESO-1 and/or LAGE-1a positive relapsed refractory multiple myeloma (RRMM).	• Adverse events (AEs and Treatment Limiting Toxicity (TLT) rate), including serious adverse events (SAEs); laboratory assessments, including chemistry, hematology, and coagulation; and cardiac assessments by electrocardiogram (ECG).
Secondary Objectives	**Secondary Endpoints**
• To describe the antitumor activity of autologous genetically modified T-cells (NY-ESO-1c259T) alone (Arm 1) or in combination with pembrolizumab (Arm 2) in participants who are HLA-A*02:01, HLA-A*02:05, and/or HLA-A*02:06 positive and have NY-ESO-1 and/or LAGE-1a positive RRMM.	• Overall Response Rate (ORR). • Time to Response (TTR). • Duration of Response (DoR) for participants who achieve at least a Partial Response (PR). • Progression-free survival (PFS).
• To describe persistence of autologous genetically modified T-cells (NY-ESO-1c259T) over time.	• Maximum persistence (Cmax), time to Cmax (Tmax), and area under the time curve from zero to time t (AUC(0-t)), as data permit.

Exploratory Objectives	Exploratory Endpoints
• To describe the antitumor activity of autologous genetically modified T-cells (NY-ESO-1^{c259}T) alone (Arm 1) or in combination with pembrolizumab (Arm 2) in participants who are HLA-A*02:01, HLA-A*02:05, and/or HLA-A*02:06 positive and have NY-ESO-1 and/or LAGE-1a positive RRMM.	• Overall survival (OS).
• To evaluate minimal residual disease (MRD) at 4 months post T-cell infusion (Week 15).	• MRD Rate at Week 15.
• To evaluate the persistence, phenotype, and functionality of NY-ESO-1^{c259} positive T-cells.	• Correlate persistence, phenotype, and functionality of NY-ESO-1^{c259}T in the peripheral blood and/or bone marrow with response to treatment and safety.
• To understand mechanisms of resistance to NY-ESO-1^{c259}T.	• Determine whether loss of NY-ESO-1 and/or LAGE-1a expression in myeloma cells is a resistance mechanism. • Correlate apparition of anti-NY-ESO-1^{c259}T antibodies with efficacy and safety. • Correlate expression of PD-L1 in the tumor microenvironment and PD-1 expression on T-cells with response to treatment. • Correlate frequency of immune cell subsets in peripheral blood and/or bone marrow with treatment response. • Correlate frequency of immune cell subsets in peripheral blood and in bone marrow.
• To evaluate antigen spreading as a mechanism of response.	• Correlate clonal outgrowth of T-cell populations with tumor response following T-cell infusion.
• To evaluate cytokine levels pre- and post-infusion on cytokine release syndrome (CRS).	• Correlate cytokine levels with incidence and severity of CRS or other safety events.
• To evaluate the impact of germline polymorphisms in IL-6, TNF-α, IL-10, IFN-γ and TGF-β on CRS.	• Correlate polymorphisms in germline deoxyribonucleic acid (DNA) with CRS.

2.3. Study Design

Overview of Study Design and Key Features



Overview of Study Design and Key Features	
Design Features	• This is a 2-arm, open-label, pilot study, with 3 distinct parts: (1) Eligibility Screening, (2) Leukapheresis/Manufacturing, and (3) Lymphodepletion/Treatment, with Parts 2 and 3 collectively representing the Treatment Phase. • Participants will first undergo screening for HLA-type (HLA-A*02:01, HLA-A*02:05, and/or HLA-A*02:06) and presence of antigen NY-ESO-1 and/or LAGE-1a in their bone marrow. Only participants who are selected after HLA-genotyping and determination of antigen expression will be considered for further eligibility screening. • In the initial study design, participants meeting all eligibility criteria were assigned to 1 of 2 treatment arms: NY-ESO-1^{c259}T alone (Arm 1) or NY-ESO-1^{c259}T in combination with pembrolizumab (Arm 2). Following protocol amendment 5, the enrolment of participants in Arm 1 will be completed before the enrolment of participants in Arm 2 continues. • Following enrolment, participants will undergo leukapheresis to obtain cells for the manufacture of autologous NY-ESO-1^{c259} bearing T-cells. • When NY-ESO-1^{c259}T-cells are available, participants will undergo lymphodepleting chemotherapy with fludarabine and cyclophosphamide and receive granulocyte-colony stimulating factor (G-CSF) support before undergoing infusion of NY-ESO-1^{c259}T-cells. • Re-confirmation of eligibility and baseline assessments will occur during the 7 days preceding lymphodepleting chemotherapy. • Participants may receive anticancer therapy between screening and leukapheresis and between leukapheresis and lymphodepletion, with mandatory wash-out periods respected. • Ten participants per arm (20 participants in total) are targeted to be enrolled in the study and receive the NY-ESO-1^{c259}T infusion, with at least 6 participants per arm having received and failed BCMA-based therapy (CAR-T, ADC, or other types of BCMA-targeted therapies) between screening and leukapheresis and/or between leukapheresis and lymphodepletion. • Eligible participants who do not receive the NY-ESO-1^{c259}T infusion for any reason will be replaced, and infused participants in Arm 2 who do not receive pembrolizumab will be included in Arm 1 for purposes of analysis and replaced within Arm 2. Analyses describing the Intent-to-Treat (ITT) population will summarize by the treatment group to which the participant was assigned. • A participant will be considered to have completed the treatment part of the study at the earliest of confirmed disease progression (with minimum 9 weeks of follow-up for safety), 108 weeks after NY-ESO-1^{c259}T-cell infusion, or death.

Overview of Study Design and Key Features	
	• After treatment, participants will be rolled into a long-term follow-up (LTFU) study under a separate protocol and followed at month 3, 6, and 12, then every 6 months for 5 years, and then yearly for up to 15 years. If the LTFU protocol is not available, follow-up will start on this protocol following the guidelines listing above until the LTFU becomes available.

Dosing	• The 2 investigational products (IPs) in this study are:
	  • NY-ESO-1^{c259}T: An autologous T-cell transduced with a self-inactivating lentivirus encoding for a high affinity NY-ESO-1/LAGE-1a-specific T-cell receptor (TCR), administered through a single IV infusion (cell range: 1×10^9 to 8×10^9 transduced cells) in both treatment arms.
	  • Pembrolizumab: A humanized monoclonal antibody, administered as a fixed dose of 200 mg through a 30-minute IV infusion in Arm 2.
	• Participants in both arms who have been re-confirmed as eligible during the baseline assessment period (Day -14 to -8) will undergo lymphodepleting chemotherapy with fludarabine (30 mg/m^2/day) on Days -8, -7, -6, and -5 and cyclophosphamide (900 mg/m^2/day) on Days -7, -6, and -5, followed by G-CSF support on Day -4 and infusion of NY-ESO-1^{c259}T-cells on Day 1.
	• For participants in Arm 2, pembrolizumab will be administered on Day 22 (Week 3; 21 days after NY-ESO-1^{c259}T infusion) and then every 3 weeks thereafter up to Week 108. If the participant experiences toxicity preventing Week-3 dosing of pembrolizumab, the first dose of pembrolizumab may be administered on Week 6 instead. If toxicity still prevents starting pembrolizumab dosing at Week 6, the participant will not be administered pembrolizumab and will be followed as a participant in Arm 1.

Time & Events	• Refer to Appendix 2: Schedule of Activities

Treatment Assignment	• Participants meeting all eligibility criteria will be treated in one of two treatment arms:
	  • Arm 1: Participants will receive NY-ESO-1^{c259}T alone as a single infusion on Day 1, 4 days after completing fludarabine, cyclophosphamide, and G-CSF (there is no Day 0 for this study).
	  • Arm 2: Participants will receive NY-ESO-1^{c259}T in combination with pembrolizumab. NY-ESO-1^{c259}T will be administered as a single infusion on Day 1, 4 days after completing fludarabine, cyclophosphamide, and G-CSF. Pembrolizumab will be administered first on Day 22 (Week 3) and then every 3 weeks thereafter up to Week 108.
	• Eligible participants who do not receive the NY-ESO-1^{c259}T infusion for any reason will be replaced, and infused participants in Arm 2 who do not receive pembrolizumab will be included in Arm 1 for

Overview of Study Design and Key Features	
	purposes of analysis and replaced within Arm 2. Analyses describing the Intent-to-Treat (ITT) population will summarize by the treatment group to which the participant was assigned. • The study initially was initially designed to randomize participants to the two arms. Following protocol amendment 5, the enrolment of participants in Arm 1 will be completed before the enrolment of participants in Arm 2 continues.
Safety Monitoring Review for TLTs	• Safety will be assessed at each clinic visit. A Safety Review Team (SRT) may review safety data in both treatment arms at any time. • TLTs will be evaluated for participants in Arm 2 only. • Enrolment in Arm 2 will be paused after the third enrolled participant has initiated lymphodepleting chemotherapy. A complete safety review of the first 3 Arm 2 participants will be conducted before enrolment resumes. • The SRT may recommend pausing the study at any time to evaluate safety and, if warranted, to close an arm of the trial (e.g., in Arm 2, if at an interim assessment the predictive probability that the TLT rate for participants exceeds 33%, is greater than 50%). • Interim analyses to inform internal decision-making may be performed for each arm after enrolment to the arm is complete and all enrolled participants in that arm who will receive NY-ESO-1^{c259}T have done so and have completed at least 3 disease assessments since infusion, progressed (if progressed prior to Week 9, then have been followed for safety for at least 9 weeks following infusion), died, or withdrawn from the study. Additional analyses may be undertaken when all participants in Arm 1 satisfy the criteria for primary analysis. Given accrual to the study was stopped prior to completing enrolment to either arm, this interim analysis will not occur.

2.4. Statistical Analyses

This study is not powered to compare safety or efficacy between the 2 treatment arms. Therefore, no hypothesis testing or formal statistical comparisons are planned. All analyses will be descriptive in nature. Continuous data will be summarized, minimally, using n, means, medians, standard deviations, and ranges, while categorical data will be summarized using frequency counts and percentages or proportions. Graphical summaries of the data will be presented, as appropriate. Time-to-event endpoints will be summarized as the median and 25th and 75th percentiles and displayed graphically using Kaplan-Meier (product-limit) curves, if the data warrant.

3. PLANNED ANALYSES

3.1. Safety Monitoring Review for TLTs

After the third participant in Arm 2 has initiated lymphodepleting chemotherapy, enrolment will be paused. Enrolment may resume after these participants have received both T-cells and pembrolizumab and a complete safety review by the SRT of Treatment-Limiting Toxicities (TLT) has been conducted.

Additionally, safety review for the assessment of TLTs may be carried out at any time in Arm 2. The SRT may recommend pausing the study to evaluate safety and, if warranted, stopping the trial (e.g., if the predictive probability of the TLT rate exceeding 33% is greater than 50%).

3.1.1. Predictive Probabilities

Predictive probabilities will be estimated for participants in Arm 2 only.

As participants are accrued and at n≥3 participants, Bayesian predictive probabilities will be used to evaluate TLTs in Arm 2. If , the probability of the end-of-trial TLT rate exceeding 0.33 is greater than 0.50 at an interim assessment (i.e., when n < [Nmax = 10]), then the SRT may recommend to pause the study for safety review and, if warranted, to stop the trial for safety.

To evaluate the TLT rate using a Bayesian framework, let p denote the TLT rate for Arm 2, and let X denote the number of TLTs in n≥3 participants. X is assumed to follow a binomial distribution B(n, p). Assuming a non-informative prior distribution of beta (0.18, 0.82) for the TLT rate, the posterior of the TLT rate will follow a beta (0.18+x, 0.82+n-x) distribution.

Let Y represent the number of TLTs in m (equal to $N_{max} - n$) future participants. With the aforementioned prior and likelihood, Y follows a beta-binomial (m, 0.18+x, 0.82+n-x) distribution. This distribution will be explored to better estimate the probability of observing y (0 [zero] to m) TLTs in the m future participants.

Let the predictive probability (PP) equal the probability of the end-of-trial TLT rate exceeding 0.33, given the maximum planned sample size (N_{max}) of 10. Using results from the first n participants, a defined θ=0.9, and methods described by Lee and Liu (Lee, 2008), PP will be computed as the weighted average (i.e., weighted by the probability of the realization of each *Y*) as? the indicator of a positive trial (i.e., at each Y, the probability of TLT rate > 0.33 is greater than 90%), should the current trend continue and the trial be conducted until the end of the study.

Refer to Table 1 below for the calculated PP associated with $n < N_{max}$. If at least 2 of the first 3 participants experience a TLT, the trial should be paused to further evaluate safety. Similarly, the trial may be paused for safety evaluation if at least 3 of the first 4 or 5 participants, at least 4 of the first 6 or 7 participants, or at least 5 of the first 8 or 9 participants experience a TLT.

Table 1 Predictive Probabilities for N_{max} = 10

	X=0	X=1	X=2	X=3	X=4	X=5	X=6	X=7	X=8	X=9
n=3	0.0017	0.115	0.566	0.9426	NA	NA	NA	NA	NA	NA
n=4	0.0002	0.0341	0.3083	0.7812	0.9842	NA	NA	NA	NA	NA
n=5	0	0.0059	0.1255	0.5447	0.9165	0.9974	NA	NA	NA	NA
n=6	0	0	0.0298	0.2932	0.7678	0.9813	1	NA	NA	NA
n=7	0	0	0	0.0956	0.5305	0.9279	1	1	NA	NA
n=8	0	0	0	0	0.2406	0.7954	1	1	1	NA
n=9	0	0	0	0	0	0.518	1	1	1	1

Furthermore, if the threshold exceeds 0.5, as described above, other supportive information may be computed. For example, the PP distribution may also be evaluated to calculate the probabilities associated with specific outcomes. For instance, if 4 of 7 participants experience a TLT, then the beta-binomial (3, 4.18, 3.82) will be used to compute the probability of observing TLTs in 1 or more of the remaining 3 participants, the average number participants with at least one TLT, the variability around these estimates, etc. In addition, the 95% credible interval for the TLT rate will be derived from the posterior distribution. These and other characteristics of the posterior distribution and posterior predictive distribution may aid in the evaluation of TLT rates.

3.2. Interim Analyses

Protocol Section 11.2 states that interim analyses to inform internal decision-making may be performed for each arm after enrolment to the arm is complete and all enrolled participants in that arm who will receive NY-ESO-1^{c259}T have done so and have completed at least 3 disease assessments since infusion, progressed (if progressed prior to Week 9, then have been followed for safety for at least 9 weeks following infusion), died, or withdrawn from the study. Additional analyses may be undertaken when all participants in Arm 1 satisfy the criteria for primary analysis.

Note that such an interim analysis is not planned and thus is not listed as a deliverable in Appendix 12: List of Data Displays.

3.3. Final Analysis

The final analyses will be performed after the completion of the following sequential steps:

1. All participants have completed the study or have withdrawn from the study for any reason. A participant will complete the treatment phase of the study upon disease progression, death, or 108 weeks after NY-ESO-1^{c259}T-cell infusion, whichever is sooner. All infused participants will enter a LTFU protocol. Study completion occurs when all participants in the treatment phase of the study have rolled over to the LTFU protocol GSK208750 (ADP-0000-002), completed long-term follow-up in this study, expired, or withdrawn (including lost to follow-up) from the parent study before rollover to the LTFU protocol
2. All required database cleaning activities have been completed and final DBR and DBF has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who signed the screening informed consent form.	• Screen failures
Enrolled	• All participants who underwent leukapheresis, with treatment arm identified as the assigned (planned) arm.	• Required study population displays (see Appendix 12: List of Data Displays for specific displays)
Intent-To-Treat (ITT)	• All participants who underwent leukapheresis, with treatment arm identified as the assigned (planned) arm.	• Study population • Primary safety (where appropriate)
Modified Intent-To-Treat (mITT)	• All participants in the ITT Population who received the NY-ESO-1^{c259}T infusion, with treatment arm identified as the arm of actual treatment received.	• Efficacy • Primary safety (where appropriate)

Refer to Appendix 12: List of Data Displays, which details the population to be used for each display. Note that, if an analysis is planned for both the mITT and ITT Population and these populations contain the same participants in the same arms, then results will be reported for the mITT Population only.

4.1. Protocol Deviations

Protocol deviations will be tracked in accordance with the Protocol Deviation Specification Form by the study team throughout the conduct of the study and sent to the Data Manger and Biostatistics Lead in a spreadsheet. Protocol deviations will not be identified programmatically.

Inclusion/exclusion criteria deviations will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Data will be listed and summarized according to GSK reporting standards, as applicable.

5.1. Study Treatment & Sub-group Display Descriptors

Two treatment arms are included in this study (Arm 1: Participants who receive NY-ESO-1^{c259}T alone; Arm 2: Participants who receive NY-ESO-1^{c259}T in combination with pembrolizumab). As data will be displayed within summaries and listings principally by treatment arm, the table below provides an example of the treatment descriptors to be used for distinguishing the treatment arms within the displays. Actual treatment doses may differ (e.g., in the case of modified pembrolizumab dosage) but will follow the same format.

Treatment Group Descriptions	
Data Displays for Reporting	
Description	**Order in TLF**
GSK794	1
GSK794+PEMBRO	2
Total	3

All data displays (Tables, Figures & Listings) will use the term “Subject” which reflects CDISC and GSK Data Display Standards terminology.

5.2. Baseline Definitions

Unless otherwise specified, baseline values will be represented by the latest non-missing measurements (including unscheduled visits) prior to the start of lymphodepleting chemotherapy. Per protocol, baseline assessments should occur within the 7 days preceding lymphodepletion. If an assessment is not performed within the 7-day window, then the latest assessment prior to the 7-day window will be used. If an assessment is performed on the same date as the start of lymphodepletion and the time of assessment is not recorded, then the assessment will be assumed to have occurred prior to lymphodepletion and used as baseline.

For ECG parameters, if baseline values are missing (given the aforementioned baseline definition of latest record within the 7 days preceding lymphodepletion), then baseline values will be represented by the mean of values recorded during the screening and Day 1 pre-dose assessments.

For participants who do not receive lymphodepleting chemotherapy during the study, baseline values will be represented by the latest, non-missing measurements recorded. If baseline data is missing, then no derivation will be performed, and baseline will be set to missing.

5.3. Multicentre Studies

Data from all participating centres will be pooled prior to analyses.

It is anticipated that participant accrual will be spread thinly across centres. Consequently, data summaries by centre are unlikely to be informative and will not be provided.

5.4. Examination of Covariates, Other Strata and Subgroups

No covariates or strata will be incorporated into analyses, and no subgroup analyses will be performed in this study.

5.5. Multiple Comparisons and Multiplicity

No formal statistical testing will be performed; therefore, no adjustments for multiple comparisons or multiplicity are planned.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the following appendices:

Section	Component
14.3	Appendix 3: Assessment Windows
14.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
14.5	Appendix 5: Data Display Standards & Handling Conventions
14.6	Appendix 6: Derived and Transformed Data
14.7	Appendix 7: Reporting Standards for Missing Data
14.8	Appendix 8: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

Study population analyses will be based on the ITT Population, unless otherwise specified. Some study population analyses will be repeated in the mITT population. If the mITT and ITT Populations contain the same participants in the same arms, then results planned for both the ITT & mITT populations will only be reported for the mITT Population.

Based on GSK Core and Oncology Data Standards, study population analyses will include summaries and listings of participant disposition, protocol deviations, demographic and other baseline characteristics, prior and concomitant medications, study treatment exposure, disease characteristics at initial diagnosis and screening, and prior and on-study anti-cancer therapies, prior anti-cancer radiotherapy, and prior and on-study surgical procedures. Details of the planned displays are presented in Appendix 12: List of Data Displays.

6.2. Disposition of Participants

Using the Screened Population, a summary and a listing of screening status and reasons for screen failure will be provided. A summary of the number of participants in each analysis population (see Section 4 for definitions) and a listing of participants excluded from each population will also be provided detailing reason for exclusion.

Overall study disposition, including transfer to the separate LTFU protocol GSK208750, will be summarized.

Treatment phase status for both arms will be summarized with reasons for non-completion as captured in the eCRF.

Listings of data describing reasons for study withdrawal and study treatment status will be produced, with the latter including dates and times, associated with leukapheresis, lymphodepletion, and T-cell infusion, dose level of T-cell infusion, indicators of treatment phase completion (vs. discontinuation), end of study status, and reasons for treatment phase discontinuation.

A summary and listing of pembrolizumab treatment status and reasons for discontinuation will be generated for participants in Arm 2.

Lastly, the number of participants in the Enrolled Population will be listed by country and study site ID.

6.3. Protocol Deviations

Important protocol deviations will be summarized and listed.

A separate listing of inclusion/exclusion deviations will also be provided.

6.4. Demographic and Baseline Characteristics

Demographic characteristics, including race, age, ethnicity, sex, height, baseline body weight, body mass index (BMI), and body surface area (BSA) as per the Mosteller formula, will be both summarized and listed. Age, height, weight, BMI, and BSA will be summarized as continuous variables, while age, sex, race, and ethnicity will be summarized as categorical variables. Age will be categorized and summarized using the GSK IDSL standard (≤18, 19-64, and ≥65 years), and in a separate summary, using EudraCT (18-64, 65-84 and ≥85 years). Age will be derived per Section 14.6.2.

Separate summaries and listings of disease characteristics at initial diagnosis and at screening will be provided. Disease characteristics including time from initial diagnosis to screening ICF signed (in months), stage at diagnosis, histologic type, percent clonal bone marrow plasma cells, presence and type of end organ damage, presence and type of plasmacytoma, presence of bone lesion(s), and chromosomal aberrations will be summarized and listed. Disease characteristics at screening will include type of multiple myeloma, HLA-A status, NY-ESO-1 status, LAGE-1a status, number of systemic therapy regimens prior to leukapheresis, number of radiotherapy regimens prior to leukapheresis, receipt of stem-cell transplant prior to leukapheresis (Y/N), and subtype of stem-cell transplant received (autologous or allogeneic). Listings will additionally disclose relevant dates (e.g., diagnosis date, dates of antigen testing). Derivation of the number of prior systemic therapy regimens should include therapies recorded as systemic therapy, as well as stem cell therapy and associated conditioning chemotherapy as a prior line. Time from initial diagnosis to screening ICF signed (in months) will be calculated as detailed in Appendix 6.

Medical conditions (history and ongoing) at screening will be listed and summarized.

6.5. Prior and Concomitant Medications

All concomitant medications will be summarized (for the mITT Population only), and all prior and concomitant medications will be included in a single listing. The definitions of prior and concomitant medications are provided in Appendix 4: Study Phases and Treatment Emergent Events.

Medications will be coded using GSK Drug coding dictionary. The summary of concomitant medications will show the number and percentage of participants taking concomitant medication by Ingredient. Multi-ingredient products will be summarized by their separate ingredients rather than as a combination of ingredients. Anatomical Therapeutic Chemical (ATC) classification Level 1 (Body System) information will be included in the dataset created but will not appear on the listing or summary.

In the summary of concomitant medications, each participant will be counted once per unique ingredient. For example, if a participant takes Amoxycillin on 2 separate occasions, the participant will be counted only once under the ingredient “Amoxycillin”. In the summary of concomitant medications, ingredients will be summarized by the base only.

Data describing concomitant receipt of blood products will be both summarized and provided in a listing.

6.6. Study Treatment Exposure

Study treatments – described in Section 5 of the protocol – are leukapheresis, lymphodepleting chemotherapy, NY-ESO-1^{c259}T cell infusion, and pembrolizumab.

The number and percentage of participants having undergone leukapheresis, lymphodepleting chemotherapy, T-cell infusion (overall and given the minimum dose of 1 x 10^9 transduced cells), and pembrolizumab infusion will be summarized.

The total number of transduced T-cells will be summarized as both a continuous variable and categorical variable. Categories will include <1, 1 to ≤8, and >8 (x 10^9 cells) and <1, 1 to ≤3, >3 to ≤8, and >8 (x 10^9 cells). An associated listing will provide T-cell infusion start/stop dates/times (over all bags), average vector copy number per cell in cell product, total number of transduced cells, and percentage of cells transduced.

For participants in Arm 2, pembrolizumab dose intensity (mg/3 weeks) and number of pembrolizumab cycles received will be listed. A listing, disclosing the details of pembrolizumab exposure, will also be generated. Additionally, a listing will be provided for all dose delays experienced on the study and duration of delay. Duration of delays is defined as period from the expected start date of dose to actual start date of current dose. The calculation of duration of delay is actual start date of current dose - expected start date of dose. Expected start date of dose = actual start date of previous dose + 21. Note that the expected start date of the first dose of pembrolizumab is 21 days after T-cell infusion. Thus, if this dose is not received, this will be considered a dose delay.

Dose administration data for lymphodepleting chemotherapy, including fludarabine and cyclophosphamide, will be presented in a single data listing. Lastly, a single participant-level data listing will be dedicated to disclosing dates of leukapheresis, lymphodepleting chemotherapy, T-cell infusion, and pembrolizumab infusion.

6.7. Anti-Cancer Therapies

Number and percentage of participants who receive any anti-cancer therapy (including systemic therapy and radiotherapy) or cancer-specific surgery will be provided in separate summaries. Systemic therapy drugs will be coded using the GSK Drug coding dictionary, then summarized by ingredient. Participant-level data describing all anti-cancer therapies and cancer-specific surgeries will be provided in separate listings.

6.7.1. Prior Anti-Cancer Therapies

Anti-cancer therapies will be classified into prior and on-study phases as described in Appendix 4. Note that only therapies initiated on or after the first day of lymphodepletion chemotherapy are considered on-study. Prior therapies will be further classified into subphases at date of leukapheresis.

Prior therapy types will include systemic therapy (including stem cell therapy), radiotherapy, and cancer-related surgery, with systemic therapies other than stem cell therapy coded using the GSK Drug coding dictionary. While all therapy types will be described within each of the aforementioned summaries, the details of each therapy type will be provided in separate listings.

Summaries of the numbers of radiotherapy and systemic anti-cancer regimens received prior to leukapheresis will be presented as part of the summary of disease characteristics at screening.

Systemic anti-cancer therapy regimens initiated between leukapheresis and lymphodepletion (as defined in Appendix 4) will be categorized as either bridging (regimens administered to maintain/stabilize the participant until T-cell infusion) or full lines (regimens administered with the intent of disease effect) by GSK physician review.

Bridging therapies will be excluded from summaries of prior anti-cancer therapy.

Thus, unless otherwise stated, summaries of prior systemic anti-cancer therapies will include all therapies before lymphodepletion except those in the leukapheresis to lymphodepletion period identified as bridging therapies. (Note that this is equivalent to all therapies prior to leukapheresis plus therapies initiated between leukapheresis and lymphodepletion identified as full lines.)

A breakdown of the number of participants who received each type of prior anti-cancer therapy will be presented.

Anti-cancer therapy will be coded using GSK Drug coding dictionary. The number of participants receiving prior anti-cancer therapies will be summarized by ATC Level 1 and ingredient. Bridging therapies will be similarly summarized.

A summary of the number of overall systemic prior anti-cancer therapy regimens and radiotherapies prior to lymphodepletion will also be produced. Systemic therapy regimens will not be broken down by type of systemic therapy since different types of therapies are expected within a regimen.

All prior anti-cancer therapy will be listed with subphase indicated and bridging therapies flagged.

All anti-cancer radiotherapy (including on-study) will be listed, with phase and subphase indicated.

All prior cancer related surgical procedures will be listed, with subphase indicated. Those before lymphodepletion will be summarized by intent and site.

6.7.2. On-Study Anti-Cancer Therapies

The number and percentage of participants who receive any anti-cancer therapy (including systemic therapy, radiotherapy, and stem cell therapy) or cancer-specific surgery will be provided in separate summaries. Systemic therapy drugs will be coded

using the GSK Drug coding dictionary, then summarized by ingredient. Participant-level data describing all anti-cancer therapies and cancer-specific surgeries will be provided in separate listings.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

All efficacy analyses are planned to be performed by treatment arm and overall. Efficacy Analyses will be conducted according to International Myeloma Working Group (IMWG) (2016) Criteria [Kumar 2016, Section 13].

7.1.1. Primary Endpoint/Variable: Overall Response Rate (ORR)

With minimal exception (see description of Confirmed Response below), only disease assessments occurring from the start of NY-ESO-1^{c259}T infusion to the earlier of confirmed progressive disease (PD) or initiation of new anti-cancer therapy (including only systemic therapy) will be considered. Note that while considered a primary endpoint for the purposes of efficacy analysis in this RAP, ORR is defined as a secondary objective in the protocol.

7.1.1.1. Best Overall Response

The BOR is defined as the best confirmed response (stringent Complete Response [sCR] > Complete Response [CR] > Very Good Partial Response [VGPR] > Partial Response [PR] > Minimal Response [MR] > Stable Disease [SD] > Progressive Disease [PD] > Not Evaluable [NE]) from treatment start date until disease progression or initiation of new anti-cancer therapy (including only systemic therapy), whichever is earlier, as assessed per IMWG (2016). Participants with only assessments of not evaluable (NE) or missing response will be treated as non-responders (i.e., they will be included in the denominator when calculating BOR percentages and the proportion representing ORR).

7.1.1.2. Overall Response Rate

The primary efficacy endpoint is ORR, defined as the percentage of participants with a best overall response (BOR) of confirmed stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) per IMWG (2016). Details regarding derivation of confirmed response are provided in Table 2.

7.1.1.3. Definition of Adequate Assessment

An adequate assessment for purposes of identifying BOR and computing ORR is defined as a disease assessment with Investigator-assessed response of sCR, CR, VGPR, PR, MR, SD, or PD per IMWG (2016). This definition of adequate assessment differs from that used for time-to-event endpoints (see Section 7.2, Secondary Efficacy Analyses).

7.1.1.4. Date Associated with Response

A disease assessment may occur at a scheduled or unscheduled visit. While the date of assessment recorded on the Disease Assessment eCRF may or may not exactly match the dates of all procedures supporting the assessment and associated with the visit, it will be used to represent the date of response.

7.1.1.5. Confirmed Response

An individual Investigator-assessed response must be confirmed at a subsequent disease assessment. Details describing the derivation of a confirmed response are provided below and in Table 2.

Pertaining to the responses of sCR, CR, VGPR, PR, and MR, a confirmed response is an Investigator-assessed response that has been documented at the confirmed response level or better across 2 consecutive adequate disease assessments (referred to as "first assessment" and "subsequent assessment"). First and subsequent disease assessments are consecutive, representing a dual-assessment scenario. The subsequent assessment is defined as the next adequate assessment (i.e., not missing or with NE response) following the first assessment, before (or on the same date of) start of new anti-cancer therapy (except for confirmation of PD, for which PD or death due to disease under study after new anti-cancer therapy may be confirmation of PD). No minimal time interval is required for the subsequent disease assessment, but a different sample is required for confirmation. If 2 consecutive assessments are performed on different dates, the assumption will be made that the 2 assessments are based on different samples.

- Note that, for participants who receive subsequent anti-cancer therapy, no imputation will be performed for completely missing start dates. However, if the start date of the anti-cancer therapy is partial (i.e., either missing the day but has the month and year available or missing both day and month), then the imputation rules described in Section 14.7.2.1, Handling of Missing and Partial Dates, will be applied.

Table 2 Response Confirmation Algorithm

Response Documented at the First Assessment[1]	Response Documented at the Subsequent Assessment	Confirmed Response Associated with the First Assessment[1]
sCR	sCR	sCR
sCR	CR	CR
CR	sCR/CR	
sCR/CR	VGPR	VGPR
VGPR	sCR/CR/VGPR	
sCR/CR/VGPR	PR	PR
PR	sCR/CR/VGPR/PR	
sCR/CR/VGPR/PR	MR	MR
MR	sCR/CR/VGPR/PR/MR	
sCR/CR/VGPR/PR/MR/SD	SD/PD/NE OR No subsequent disease assessment prior to new anti-cancer therapy, if any (participant may or may not still be on study)	SD
PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion)	PD (any reason), including PD after initiation of new anti-cancer therapy OR	PD

Response Documented at the First Assessment[1]	Response Documented at the Subsequent Assessment	Confirmed Response Associated with the First Assessment[1]
	No subsequent disease assessment: participant died due to disease under study before further adequate assessment could be performed (including death due to disease under study after initiation of new anti-cancer therapy)	
PD due to imaging (i.e., plasmacytoma or bone lesion)	Any OR No subsequent disease assessment	
PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion)	sCR/CR/VGPR/PR/MR/SD OR No subsequent disease assessment	NE
NE or missing	Any OR No subsequent disease assessment	

[1] The date of confirmed response for all scenarios equals the date associated with the first disease assessment.

7.1.2. Summary Measurement

The number and percentage of participants in the following best confirmed response categories will be summarized: sCR, CR, VGPR, PR, overall response (sCR+CR+VGPR+PR), MR, SD, PD, and NE. Corresponding 2-sided exact (Clopper-Pearson) 95% CIs for ORR will also be provided for each arm and total. Participants with unknown or missing responses will be considered NE.

A participant-level data listing of Investigator-assessed responses per assessment timepoint, visit level response, and BOR will be provided, including the name of the corresponding visit, date of the response assessment, study day, and observed response.

A spider plot for the change from baseline over time and a waterfall plot showing the maximum percent reduction from baseline will be produced for Serum M-protein, Urine M-protein and Serum free light chain (FLC), if data warrant. The maximum percent reduction will be plotted in the following hierarchical order:

(1) Plot Serum M-protein maximum percent reduction from baseline, if data are available;

(2) If (1) is not feasible, plot Urine M-protein maximum percent reduction from baseline, if data are available;

(3) If both (1) and (2) are not feasible, plot maximum percent reduction from baseline for difference between 2 types of Serum FLC, if data are available.

Difference between 2 types of Serum FLC

The percent change from baseline for difference between 2 types of Serum FLC is defined as:

(post-baseline difference – baseline difference) / baseline difference x 100.

To calculate the difference, the "involved" and "non-involved" light chains must be determined first, based on the ratio of non-missing values for Serum Kappa FLC protein and Serum Lambda FLC protein at baseline.

The detailed algorithm is provided as below:

- If the baseline ratio of (Kappa FLC/Lambda FLC) > 1.65, then Kappa FLC is defined as involved FLC, and Lambda FLC is defined as non-involved FLC. Then:
  - Difference between involved and uninvolved = Kappa FLC – Lambda FLC.
- If the baseline ratio of (Kappa FLC/Lambda FLC) < 0.26, then Lambda FLC is defined as involved FLC, and Kappa FLC is defined as non-involved FLC. Then:
  - Difference between involved and uninvolved = Lambda FLC – Kappa FLC.
- If the baseline ratio of (Kappa FLC/Lambda FLC) ≥ 0.26 and ≤ 1.65, then "involved" and "non-involved" FLC cannot be determined (ratio is normal), and calculation of the maximum percent reduction from baseline for the difference between 2 types of Serum FLC will not be possible.

7.1.3. Population of Interest

The mITT Population will support the primary efficacy analyses, while the ITT Population will be used for sensitivity analysis of the primary efficacy endpoint. If the mITT and ITT Populations are identical, then only the results associated with the mITT Population will be reported.

7.1.4. Strategy for Intercurrent Events

A composite strategy will be followed for participants who are not evaluable or have missing BOR who will be treated as non-responders; i.e., they will be included in the denominator when calculating the percentage.

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and based on GSK data standards and statistical principles.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoints/Variables

7.2.1.1. Time to Response (TTR)

TTR is defined as the time interval (in months) from T-cell infusion to initial date of documented confirmed response (PR or better) in the subset of participants who showed a confirmed BOR of PR or better by Investigator assessment per IMWG (2016).

7.2.1.2. Duration of Response (DoR)

DoR is defined as the time interval (in months) from initial date of documented confirmed response (PR or better) to the date of confirmed PD or death due to disease under study for participants who showed a confirmed BOR of PR or better IMWG (2016).

Although documentation of responses of PR and better requires a confirmatory measurement, the start time for DoR will be the first date on which response was noted (i.e., the date of "first assessment", as described in Section 7.1.1, Primary Endpoint/Variable: Overall Response Rate (ORR)). Determination of event/censoring for DoR events and associated dates are described in Table 3.

Note that, for participants who receive subsequent anti-cancer therapy, no imputation will be performed for completely missing start dates. However, if the start date of the anti-cancer therapy is partial (i.e., either missing the day but has the month and year available or missing both day and month), then the imputation rules described in Section 14.7.2.1, Handling of Missing and Partial Dates, will be applied.

Table 3 Assignments for Progression/Death and Censoring Dates for DoR Analysis

Scenario	Date of Event or Censoring	Event or Censored
No (or inadequate) baseline assessment[1] and the participant has not died (if the participant has died, follow the rules for death at the bottom of this table).	Date of T-cell infusion	Censored
No post-baseline assessments and the participant has not died (if the participant has died, follow the rules for death at the bottom of this table).	Date of T-cell infusion	Censored
New anti-cancer therapy started on or after lymphodepletion and prior to T-cell infusion	Date of T-cell infusion	Censored
PD documented at or between scheduled visits.	Date of documented PD[3]	Event

Scenario	Date of Event or Censoring	Event or Censored
With post-baseline assessment but no PD or death.	Date of last adequate disease assessment[2]	Censored
New anti-cancer therapy started prior to documented PD or death[3].	Date of last adequate disease assessment[2] on or prior to starting anti-cancer therapy	Censored
Death due to disease under study without extended loss to follow-up.	Date of death	Event
Death from causes other than disease under study without extended loss to follow-up.	Date of death	Censored
Death or PD after extended loss to follow-up of 2 or more cycles + 1/3/7-day window.	As the schedule of assessments (Myeloma markers labs) changes through the course of the protocol (i.e., starting on Week 1 and then every 3 weeks from Week 3 until Week 24 and then every 6 weeks until Week 72, then every 12 weeks until PD), the following rules will be used for identifying extended loss to follow-up or extended time without an adequate assessment (i.e., 2 or more missed assessments + window). • If death or PD is on or prior to Day 45 (= Week 6 + 3-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 37 days (= 2 weeks + 3 weeks + 1-day window + 1-day window) prior to death or PD; • Else if death or PD is after Day 45 (= Week 6 + 3-day window) and on or prior to Day 175 (= Week 24 + 7-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 48 days (= 3 weeks + 3 weeks + 3-day window + 3-day window) prior to death or PD; • Else if death or PD is after Day 175 (= Week 24 + 7-day window) and on or prior to Day 504 (= Week 72 + 7-day window), then	Censored

Scenario	Date of Event or Censoring	Event or Censored
	participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 98 days (= 6 weeks + 6 weeks + 7-day window + 7-day window) prior to death or PD; • Else if death or PD is after Day 504 (= Week 72 + 7-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 182 days (= 12 weeks + 12 weeks + 7-day window + 7-day window) prior to death or PD. DoR will be censored on the date of last adequate disease assessment prior to PD/death.[2]	

[1] Adequate baseline assessment is defined as a baseline assessment with at least one serum protein electrophoresis (SPEP), urine protein electrophoresis (UPEP), or involved FLC result available for analysis.

[2] Adequate disease assessment is defined as a disease assessment with Investigator-assessed response of sCR, CR, VGPR, PR, MR, or SD per IMWG (2016). The date of response will be recorded on the Disease Assessment eCRF.

[3] If PD (or death) and new anti-cancer therapy occur on the same day, the assumption will be made that PD (or death) was documented first (i.e., PD would equal the outcome and the relevant date would be the date of documented PD). If anti-cancer therapy is started prior to any adequate disease assessments (but after lymphodepleting chemotherapy), the censoring date will equal the date of T-cell infusion.

7.2.1.3. Progression Free Survival (PFS)

PFS is defined as the time interval (in months) between the date of T-cell infusion and the initial assessment date of confirmed PD as assessed by the investigator per IMWG (2016) or date of death due to any cause. Determination of dates of PFS events and dates for censoring are described in Table 4.

Table 4 Assignments for Progression and Censoring Dates for PFS Analysis

Scenario	Date of Event (Progression/Death) or Censoring	Event (Progression/Death) Or Censored
No (or inadequate) baseline assessment[1] and the participant has not died (if the participant has died, follow the rules for death at the bottom of this table).	Date of T-cell infusion	Censored
No post-baseline assessments and the participant has not	Date of T-cell infusion	Censored

Scenario	Date of Event (Progression/Death) or Censoring	Event (Progression/Death) Or Censored
died (if the participant has died, follow the rules for death at the bottom of this table).		
PD documented between scheduled visits, without extended loss to follow-up.	Date of documented PD[3]	Event
With post-baseline assessment but no documented PD or death.	Date of last adequate disease assessment[2]	Censored
No adequate post-baseline assessment before start of new anti-cancer therapy.	Date of T-cell infusion	Censored
With adequate post-baseline assessment and new anti-cancer therapy started prior to documented PD or death[3].	Date of last adequate disease assessment[2] on or prior to starting anti-cancer therapy	Censored
Death before first scheduled assessment, or death at baseline without adequate baseline assessment, or death following a post-baseline assessment (i.e., "between assessments") without extended loss to follow-up.	Date of death	Event
Death or PD after extended loss to follow-up or time without adequate disease assessment of 2 or more cycles + 1/3/7-day window	As the schedule of assessments (Myeloma markers labs) changes through the course of the protocol (i.e., starting on Week 1 and then every 3 weeks starting from Week 3 until Week 24 and then every 6 weeks until Week 72, then every 12 weeks until PD), the following rules will be used for identifying extended loss to follow-up or extended time without an adequate assessment (i.e., 2 or more missed assessments + window). • If death or PD is after Day 45 (= Week 6 + 3-day window) and on or prior to Day 175 (= Week 24 + 7-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 48 days (= 3 weeks + 3 weeks + 3-day	Censored

Scenario	Date of Event (Progression/Death) or Censoring	Event (Progression/Death) Or Censored
	window + 3-day window) prior to death or PD; • Else if death or PD is after Day 175 (= Week 24 + 7-day window) and on or prior to Day 504 (= Week 72 + 7-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 98 days (= 6 weeks + 6 weeks + 7-day window + 7-day window) prior to death or PD; • Else if death or PD is after Day 504 (Week 72 + 7-day window), then participant status will be labelled "extended loss to follow-up" if the participant did not have an adequate assessment during the period of 182 days (12 weeks + 12 weeks + 7-day window + 7-day window) prior to death or PD. PFS will be censored on the date of last adequate disease assessment (or T-cell infusion, if no adequate disease assessment) prior to PD/death.[2]	

[1] Adequate baseline assessment is defined as a baseline assessment with at least one serum protein electrophoresis (SPEP), urine protein electrophoresis (UPEP), or involved FLC result available for analysis.

[2] Adequate disease assessment is defined as a disease assessment with Investigator-assessed response of sCR, CR, VGPR, PR, MR, or SD per IMWG (2016). The date of response will be recorded on the Disease Assessment eCRF.

[3] If PD (or death) and new anti-cancer therapy occur on the same day, the assumption will be made that PD (or death) was documented first (i.e., PD would equal the outcome and the relevant date would be the date of documented PD). If anti-cancer therapy is started prior to any adequate disease assessments (but after starting lymphodepleting chemotherapy), the censoring date will equal the date of T-cell infusion.

7.2.2. Summary Measure

7.2.2.1. Time to Response (TTR)

Time to response for each participant with a confirmed response (PR or better) will be listed in months. Details are provided in Appendix 12.

7.2.2.2. Duration of Response

Duration of response for each participant with a confirmed response (PR or better) will be listed in months. Details are provided in Appendix 12.

7.2.2.3. Progression Free Survival

PFS will be summarized using Kaplan-Meier curves. Median PFS, first and third quartiles and 95% CI, will be estimated using the Brookmeyer-Crowley method [Brookmeyer, 1982]. A listing of PFS times and associated details will also be provided. Details of the planned displays are provided in Appendix 12.

7.2.3. Population of Interest

Secondary efficacy analyses will be based on the mITT Population.

7.2.4. Statistical Analyses / Methods

Details of the planned displays will be provided in Appendix 12: List of Data Displays and are based on GSK data standards and statistical principles. Unless otherwise specified, endpoints / variables defined above in Section 7.2.2 will be summarized by arm using descriptive statistics, graphically presented (as appropriate), and listed.

7.3. Exploratory Efficacy Analyses

MRD will not be analysed at part of this RAP.

7.3.1. Endpoints/Variables

7.3.1.1. Overall Survival (OS)

OS is defined as the time interval (in months) from the date of T-cell infusion to the date of death due to any cause.

Survival outcomes for subjects who have not died by the point of analysis will be censored on the date of last known contact with the participant.

7.3.2. Summary Measure

OS for each participant will be listed in months.

7.3.3. Population of Interest

The exploratory efficacy analysis will be based on the mITT Population.

7.3.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and are based on GSK data standards and statistical principles. Unless otherwise specified,

endpoints / variables defined in Section 7.3.1 will be summarized using descriptive statistics, graphically presented (if appropriate), and listed.

8. SAFETY ANALYSES

The safety analyses will be based on the Intent-to-Treat population except for displays that are treatment dependent where the modified Intent-to-Treat population will be used, as detailed in Appendix 12.

Unless otherwise specified, summaries will include descriptive statistics by treatment arm, as well as overall (across treatment arms).

8.1. Adverse Events Analyses

Analysis of AEs, including all AEs, serious AEs (SAEs), and other significant AEs, will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 12: List of Data Displays.

AEs will be graded according to National Cancer Institute-Common Toxicity Criteria for Adverse Events (NCI-CTCAE) version 4.03 unless otherwise specified in the protocol. For instance, the grading of AE-related Cytokine Release Syndrome (CRS) will be performed using modified NCI-CTCAE guidance developed by Lee (2019, Section 13); see protocol Table 5 and Section 8.5. For the grading of Graft versus Host Disease (GVHD) associated AEs, see protocol Section 8.6.2. AEs will be coded to the level of Preferred Term (PT) using the latest version of the Medical Dictionary for Regulatory Affairs (MedDRA).

In the eCRF for this study Adverse Events for which the grade changes over the course of the event are entered as multiple records, one record per grade. (If multiple grades are experienced on the same day then the highest grade for that day is reported.) Similarly, events where other attributes such as relatedness change over the course of the event will also be entered as multiple records. For analyses requiring summaries of numbers or characteristics of individual events, these multiple sequential segments will be collapsed back into a single event record prior to analysis using the algorithm detailed in Appendix 15

AEs related to study treatment, SAEs, SAEs related to any study treatment, fatal AEs, and fatal AEs related to any study treatment will be summarized.

Tables will summarize all AEs for the ITT population and Treatment Emergent AEs for the MITT population.

A summary of common non-serious AEs that occurred strictly in ≥5% of participants will be provided, without rounding of the percentage to overcome the 5% threshold (e.g., events with 4.9% incidence rate will not be included). This summary will display the number and percentage of participants, while a separate summary will present the total numbers of occurrences of the common non-serious AEs. Both summary tables will be displayed by MedDRA System Organ Class (SOC) and PT.

The relationship between MedDRA SOC, PT, and Verbatim Text will be listed.

A summary of number and percentage of participants with any AEs by maximum grade will be produced. AEs will be sorted by combined PT in descending order of total incidence. The summary will use the following algorithms for counting the participant:

- **Preferred term row**: Participants experiencing the same AE preferred term several times with different grades will only be counted once with the maximum grade.
- **Any event row**: Each participant with at least one AE will be counted only once at the maximum grade no matter how many events they have.

In addition, the frequency and percentage of AEs (all grades) will be summarized and displayed in 2 ways: 1) in descending order of total incidence by combined PT only and 2) in descending order of total incidence by SOC and PT. In the SOC row, the number of participants with multiple events under the same SOC label will be counted once.

A study treatment-related AE is defined as an AE for which the investigator classifies the relationship to lymphodepleting chemotherapy, T-cell infusion, and/or pembrolizumab as "Yes", which includes "Definitely Related", "Probably Related", and "Possibly Related". Summary of study treatment related AEs by combined PT and maximum grade will also be provided separately for relatedness to each study treatment. A worst-case scenario approach will be taken to handle missing relatedness data (i.e., the summary table will include events with the relationship to study treatment as 'Yes' or missing).

In addition to the summaries and listings described above, listings will be provided for all AEs, AEs leading to pembrolizumab dose interruption (in Arm 2), AEs leading to pembrolizumab dose reduction (in Arm 2), AEs leading to pembrolizumab dose discontinuation (in Arm 2), delayed AEs as adjudicated by GSK (provided from external data source), and participant IDs per individual AE.

Tables that summarize AEs by SOC and PT will use MedDRA preferred terms, as well as any adverse event tables required for disclosure. This will be detailed in the programming notes in Appendix 12: List of Data Displays. Most other AE tables will summarize AEs by using the combined terms defined in Appendix 14: Combined Preferred Terms, as detailed in the programming notes in Appendix 12: List of Data Displays.

In the event that a participant has withdrawn consent, no data after the withdrawal of consent date from this participant including death should appear in the database, which should be part of the data cleaning process. All deaths will be summarised based on the number and percentage of participants. This summary will classify participants by time of death relative to the date of T-cell infusion (>30 days or ≤30 days) and primary cause of death (disease under study, treatment related toxicity, or other). A supportive listing will be generated to provide participant-specific details on participants who died.

AEs deemed serious are those events leading to death, life-threatening circumstance, or new/prolonged hospitalization or, given appropriate medical judgement, requires medical or surgical intervention to prevent one or more of the aforementioned outcomes (see protocol Section 9.3 for more detail). Separate summaries will be provided for AEs (and SAEs) related to study treatments: one for lymphodepleting chemotherapy-related (S)AEs, one for T-cell infusion-related (S)AEs, and one for all study treatment related

(S)AEs. Summaries of fatal AEs, and fatal AEs related to any study treatment will be produced. Fatal AEs will only be summarized if there are at least 5 participants with fatal AEs.

SAEs will be included in the listing of all AEs, but also separate supportive listings with participant-level details will be generated for:

- Non-fatal SAEs
- Reasons for considering AE as serious

A summary of total incidence and frequency and percentage of grade 3, 4, and 5 events will be presented by study arm and total for the following: all AEs, all treatment emergent AEs, all study-treatment related AEs, all T-cell related AEs, all lymphodepletion related AEs, all serious AEs, and all study-treatment related, T-cell related, and lymphodepletion related serious AEs.

A plot of study duration including study days of any SAE, death, progression, and response will be produced.

8.2. Adverse Events of Special Interest (AESI) Analyses

AESIs include:

- Cytokine Release Syndrome
- Haematopoietic cytopenias (including pancytopenia and aplastic anaemia)
- Graft versus Host Disease (GvHD)
- Immune Effector-Cell Associated Neurotoxicity Syndrome (ICANS)
- Guillain-Barre Syndrome (GBS)

A focused list of MedDRA terms based on clinical review will be used to identify each type of event. In addition, all potential haematopoietic cytopenias will be identified using a comprehensive list of MedDRA terms. Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting, and emerging data from on-going studies may highlight additional AEs of special interest (AESIs). Therefore, the list of terms to be used for each event of interest and the specific events of interest will be based on the SRT agreements in place at the time of reporting. Due to expected small numbers, Gullian-Barre Syndrome, Immune Effector-Cell Associated Neurotoxicity Syndrome, and Graft versus Host Disease will only be displayed in listings. Details of the planned displays are provided in Appendix 12: List of Data Displays.

AESI tables will be reported for the mITT population.

The number and percentage of participants with these events will be summarized by categories of AESI, combined preferred term, and grade in one table using both the comprehensive list and focused list. All additional AESI tables described below will be summarized using the focused list and additional Haematopoietic cytopenia AESI tables

will also be summarized by cell line, using the specific neutropenia, thrombocytopenia, and anemia preferred terms in the focused list.

Listings of AESIs will be produced for each AESI category using the focused list, which will include leukapheresis date, lymphodepletion start date, T cell infusion date, AE start date, AE end date, SAE code, grade, relationship to study treatment and outcome of event. An additional listing of cytopenias identified in the comprehensive list will also be provided.

The summary of event characteristics for each category of AESI will also be provided, including number of participants with any event, number of events, number of participants with any event that is serious, number of participants with any event that is related to study treatment, the outcome of the event, maximum grade and the action taken for the event. The percentage will be calculated in 2 ways, one with number of participants with event as the denominator and the other with total number of participants as the denominator. The worst-case approach will be applied at participant level for the event outcome and maximum grade, i.e. a participant will only be counted once as the worst case from all the events experienced by the participant. For action taken to an event, participant will be counted once under each action, e.g. if a participant has an event leading to both study treatment discontinuation and dose reduction, the participant will be counted once under both actions.

A summary of onset and duration of the first occurrence of all AESIs will be created for each AESI separately, and for Haematopietic cytopenias this will include an overall analysis of events in the focused list of PTs for this AESI as well as separate analyses for cell lines describing events of Neutropenia, Anemia, and Thrombocytopenia. A summary of onset and duration of the last occurrence of focused list Haematopoietic cytopenias will also be created. In addition, a summary of time to resolution will be created for each AESI separately. The time to resolution displays summarize participants with an AESI occurring before study day 30. Among all AESIs occurring before study day 30, the worst-case study day of resolution will be summarized. Additionally, the worst-case AESI duration of all recurrent AESIs will be summarized. Recurrent AESI is defined as additional occurrences of AESIs after day 30, after initial occurrence and before study day 30. Duration is defined as AESI end date – AESI start date + 1.

Characteristics, Onset and Duration, and Time to Resolution summaries will not be created if there are 0 or 1 AESI in total.

8.2.1. Cytokine Release Syndrome (CRS) and Graft versus Host Disease (GvHD)

Refer to protocol Section 8.5 and Section 8.6 for the definitions and the grading of CRS and GvHD. The listing of CRS AESIs will also include time from infusion to first CRS (days) and time from infusion to max CRS (days). Listings of symptoms, medications and procedures related to CRS and GvHD will be produced separately. The mock-up shells are in Appendix 13: Example Mock Shells for Data Displays.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including chemistry, hematology, and other laboratory tests, including biomarker tests, will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 12: List of Data Displays.

The laboratory assessments to be conducted for monitoring participant safety are listed in Table 5, List of Clinical Laboratory Tests.

Table 5 List of Clinical Laboratory Tests

Clinical Chemistry	Hematology
Total Calcium	Red blood cell count
Calcium corrected for Albumin	Hemoglobin
Phosphorus	Hematocrit
Magnesium	Mean cell volume
Albumin	Mean corpuscular hemoglobin
Bilirubin	Mean corpuscular hemoglobin concentration
Alanine aminotransferase	Platelet count
Aspartate aminotransferase	White blood cell count
Alkaline phosphatase	White blood cell differential absolute counts of lymphocytes, monocytes, and neutrophils
Lactate dehydrogenase	White blood cell differential percentages of lymphocytes, monocytes, and neutrophils
Sodium	
Potassium	
Bicarbonate	
Creatinine*	
Chloride	
Glucose	
BUN or Urea	
Uric Acid	
C-reactive protein	
* In participants ≥65 years, add GFR	

Other Clinical Lab tests	
Urinalysis: Glucose Ketones Specific gravity Protein Blood Microscopy Bilirubin pH **Coagulation:** Prothrombin time or International Normalized Ratio Activated partial thromboplastin time **Endocrinology:** Thyroid stimulating hormone **Myeloma markers:** SPEP UPEP IgG IgM IgA Serum free Kappa chain Serum free Lambda chain Kappa/Lambda ratio determination Beta-2 microglobulin Serum M-protein Serum Immunofixation	**Immunology:** HIV 1+2 antibody Hepatitis B surface antigen Hepatitis B core antibody – if positive, test for HBV DNA Hepatitis C antibody – if positive, test for HCV RNA HTLV 1+2 IgG CMV IgG EBV (EBNA) Syphilis (RPR) CMV DNA PCR – peripheral blood for detection of reactivation. **Pregnancy:** Serum beta-HCG or urine test

Summaries of worst-case grade increase from baseline grade at Week 4, Week 15, and across all post-baseline visits will be provided for all the lab tests that are gradable by NCI-CTCAE v4.03. The worst grade will be derived based on all post baseline records including unscheduled visits. These summaries will display the number and percentage of participants with a maximum post-baseline grade increasing from their baseline grade. Missing baseline grade will be assumed as grade 0. For laboratory tests that are graded for both low and high values, summaries will be done separately and labeled by direction, e.g. sodium will be summarized as hyponatremia and hypernatremia.

For lab tests that are not gradable by NCI-CTCAE v4.03, summaries of worst-case changes from baseline with respect to normal range will be generated. Decreases to low,

changes to normal or no changes from baseline, and increases to high will be summarized at each scheduled visit as well as for the worst-case post-baseline. If a participant has a decrease to low and an increase to high during the same time interval, then the participant is counted in both the "Decrease to Low" categories and the "Increase to High" categories. In addition, the summary will include worst-case changes from baseline with respect to normal range for worst cases.

Separate summary tables for hematology, chemistry, and other laboratory tests will be produced. Summary of the change from baseline for hematology, chemistry, and other lab tests will be provided by visit using n, mean, median, standard deviation, minimum, and maximum. A plot of each subject's laboratory data over time will be created for the following hematologic tests: neutrophils, lymphocytes, platelets, and hemoglobin. Additionally, all laboratory values will be provided in a listing.

Detailed derivation of baseline assessment is specified in Section 5.2, Baseline Definitions. Unless otherwise specified, the denominator used in calculating percentage at each scheduled visit will equal the number of participants with non-missing values at the particular visit.

8.3.1. Analyses of Liver Function Tests (LFT)

Listings of hepatobiliary laboratory events including possible Hy's law cases will be provided in addition to what has been described above, including listings of liver monitoring and stopping events as well as a listing of subjects meeting hepatobiliary laboratory criteria post-baseline.

Possible Hy's law cases will be defined as any event of either: (a) alanine aminotransferase (ALT) ≥3 × the upper limit of normal (ULN) and bilirubin ≥2 × ULN (>35% direct bilirubin) or (b) ALT ≥3 × ULN and INR >1.5, if INR is measured. Total bilirubin ≥2 × ULN can be within 28 days following the ALT elevation and, if direct bilirubin is available on the same day, it must be ≥35% of total bilirubin. Note that INR measurement is not required, and the threshold value stated will not apply to participants receiving anticoagulants.

A scatter plot of maximum total bilirubin versus maximum ALT will be generated. Also, a scatter plot of maximum vs baseline for ALT will be produced.

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results, including ECGs and vital signs, will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 12: List of Data Displays.

8.4.1. Performance Status

Eastern Cooperative Oncology Group (ECOG) performance status at baseline and at the participant's last assessment will be summarized. A summary of change from baseline by scheduled visits will also be produced, including the worst-case and best-case post-

baseline changes during the study (improved, no change, deteriorated). Summaries will use frequency and percentage of participants at each planned assessment time. A supportive listing will also be provided.

8.4.2. ECG

A summary of the number and percentage of participants who had normal and abnormal (clinically significant and not clinically significant) ECG findings will be displayed by scheduled visits as well as for the worst-case post-baseline. The worst case will be chosen from all available ECG findings, including scheduled and unscheduled visits.

A summary of change from baseline in ECG values will be produced.

A summary of increases in QTc comparing the baseline value to worst-case post baseline value will be provided. The worst-case post baseline row is used to summarize the participants' overall worst-case shifts post baseline. The determination of the worst-case post baseline takes into account both planned and unscheduled assessments. In addition, the summary also includes a comparison of the worst-case shifts by planned time intervals.

Similarly, the amount of increase from baseline in QTc values will also be summarized. Participants with missing baseline values will be excluded from this summary.

Summaries of QTc values will incorporate corrections based on Friderica's or Bazett's formula separately (with values referred to as QTcF and QTcB, respectively).

Listings of abnormal ECG findings and a listing of ECG values will be provided.

A figure plotting QTc shift from baseline to worst-case post baseline will be produced, with separate plots for the 2 correction methods (QTcF and QTcB). Plots within the figure will have reference lines at 480 and 500 msec for both the ordinate and abscissa axes. There will be diagonal reference lines at equality (i.e., a 45-degree line), at equality plus 30 msec, and at equality plus 60 msec.

8.4.3. Pregnancies

Pregnancy (or pregnancy of a male participant's partner) is not considered an AE/SAE unless there is reason to believe that the pregnancy may be the result of failure of the contraceptive being used due to interaction with the study drug. However, the investigator shall report all pregnancies immediately to the Sponsor. If participants or participants' partner become pregnant while on the study, the information will be included in the narratives and no separate table or listing will be produced.

8.4.4. Vital Signs

A summary of change from baseline in vital signs will be provided. Also, a summary of worst-case vital signs results by Potential Clinical Importance (PCI) criteria post-baseline relative to baseline will be generated (see Appendix 8: Values of Potential Clinical Importance).

A listing of vital signs with values of PCI will be provided.

8.4.5. Replication Competent Lentivirus (RCL) and Persistence of NY-ESO-1^{c259}T

The proportion of participants who are RCL positive will be summarized. RCL is reported as "Negative" if copies of VSV-G are <50 copies/ug DNA.

RCL results will also be presented in a data listing.

The proportion of patients showing >1% gene marked peripheral blood mononuclear cells (PBMCs) one-year post-treatment will be summarized if data warrant.

For any patient who has greater than 1% gene marked PBMCs at 1 year or beyond post-infusion, integration site analysis will be performed on PBMCs to assess clonality and possible insertional oncogenesis. A summary of the number of subjects with any number of clones with >7% abundance will be summarized if data warrant. A supporting listing will be provided. Two diversity indices, Shannon diversity index and Gini index, will be reported in the data listing. These indices can help summarize the composition of a population of clones. Shannon diversity is a measurement that represents the uncertainty about the identity of a single species within the population [Shannon, 1948, Section 13]. The Gini index can help detect the similarity in abundance of different clones across the population [Gini, 1914, Section 13]

Further details of the handling of persistence data and its analysis as a biomarker are given in Section 9.1.

8.4.6. COVID-19

A listing of all COVID-19 assessments, including test date and result, along with symptom assessments will be provided.

9. PHARMACOKINETIC ANALYSES

9.1. Primary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

Evaluation of persistence of NY-ESO-1^{c259}T cells over time is a secondary objective.

9.1.1.1. Drug Concentration Measures

Spider plots will be used to graphically summarize persistence over time for each participant by responders and non-responders. Spider plots of Bone Marrow Mononuclear Cell (BMMC) persistence data will also be produced if data is available.

9.1.1.2. Derived Pharmacokinetic Parameters

The PK parameters presented in the table below will be derived during programming. This will be the responsibility of the Statistics and Programming group at PAREXEL under the direction of the Clinical Pharmacology Modeling and Simulation (CPMS) Department at GSK.

Peak expansion during the study (Cmax), time to peak expansion (Tmax), and as data permit, $AUC_{(0-28)}$ will be summarized overall and for responders and non-responders using descriptive statistics and dot plots.

The area under the plasma concentration-time curve to day 28 ($AUC_{(0-28)}$) will be determined using the linear trapezoidal rule for increasing concentrations and the logarithmic trapezoidal rule for decreasing concentrations. PK samples intended for day 28 will be treated as collected on that day provided they are collected within 4 days of day 28.

9.1.2. Summary Measure

For each of these parameters, except Tmax, the following summary statistics will be calculated: n, median, minimum, maximum, arithmetic mean, 95% confidence interval for the arithmetic mean, standard deviation, coefficient of variation (coefficient of variation (CV) = 100*(sqrt (exp(SD^2) - 1))) [NOTE: SD = SD of log transformed data]), geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data. Data will be summarized by treatment arm and overall, and by type of persistence if BMMC persistence data is available.

For Tmax, calculations will include median, maximum, minimum, arithmetic mean, 95% confidence interval, and standard deviation. Data will be summarized by treatment arm and overall.

A listing of persistence will be provided and will include coefficient of variation, number of positive replicates, copies/cell, copies/µg DNA, percent gene marked cells of PBMCs (%), interpretive result, duration of detectible persistence, time to loss of 25%/50%/75% peak expansion, and $AUC_{(0-28)}$. An identical persistence listing will be created for BMMC data.

Time to loss of 25% of peak expansion will be calculated as the time since T-cell infusion corresponding to observing at least 25% loss of peak expansion. If time to 25% loss of peak expansion is not observed, the last observed time will be reported with a "+". The same procedure will be followed for 50% and 75%.

The following calculations will be performed:

copies/cell is calculated with the following formula:

copies/cell=(copies/µg) x (0.0000063 µg gDNA/cell)

Percent gene-marked cells of peripheral blood mononuclear cells (PBMCs) = (copies/cell) x 100

The final reported result of copies/µg gDNA is calculated as follows:

copies/µg DNA=copies per well/µg gDNA per well

For persistence value below LLOQ, the following rules will be applied:

Reported Copies per cell Result	Reported Copies per ug gDNA Result	Reported Result	Set Value for Copies per cell	Set Value for Copies per ug gDNA
<0.0003	<50.0	Negative	0	0
<0.0003	<50.0	Detectable, <LLOQ	0.0003	50

Note, sometimes values for copies per cell and copies per ug DNA might be different than above as it depends on the input of DNA, but rule would be the same:

- If interpretive reported result is negative, then set values to 0.
- If interpretive reported result is “Detectable, <LLOQ”, set values to LLOQ (If <XXX, set at XXX)

The unit for persistence will be “Copies/ug of gDNA”

Duration of detectable persistence is defined as time from T-cell infusion until persistence is no longer detectable. Persistence above the assay limit of detection but below the lower limit of quantitation is considered for the duration determination, i.e. the time window from infusion until the first instance persistence falls below the detection limit and the interpretive reported result is “Negative.” If persistence for a given participant remains detectable (“Positive” or “Detectable, LLOQ”) at their last sample collection timepoint, the last observed time is reported and considered as right-censored with a “+” appended to the numerical result. Note, transduced T-cells frequently persist beyond the follow-up period, and hence, the reported duration is directly influenced by length of time the participant is on-study

9.1.3. Population of Interest

All analyses of persistence will be based on the mITT population, unless otherwise specified.

10. BIOMARKER ANALYSES

10.1. Biomarker Analyses

10.1.1. Endpoint / Variables

Anti-NYESO antibody formation will be reported if data warrant.

10.1.2. Summary Measure

10.1.2.1. Anti-NYESO-1 Antibody Formation

The anti-NY-ESO-1 antibody results, including titers, will be reported for all participants in a data listing. Additionally, the overall incidence of participants with all negative or confirmed positive results at baseline and any post-treatment time point will be summarized if data warrant.

10.1.3. Population of Interest

Biomarker analyses will be based on the mITT Population, unless otherwise specified.

10.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and are based on GSK data standards and statistical principles.

11. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Not applicable.

12. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

Not applicable.

13. REFERENCES

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14. APPENDICES

14.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Specification document.

14.2. Appendix 2: Schedule of Activities

14.2.1. Protocol Defined Schedule of Events

	Screening[a] Phase / Eligibility Phase		Treatment Phase																			DC of Pem-broli-zumab Tx[c]	Comple-tion of Treatment Phase or WD[d]
			Leukapheresis	Baseline ≤7 days prior to chemo	Lymphodepleting Chemotherapy[b]					T-cell infu-sion													
Study Day	**Scrn**	**Elig**		**D -14 to D -8**	**D -8**	**D-7**	**D -6**	**D -5**	**D -4**	**D 1**	**D2**	**D3**	**D4**	**D5**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 6**	**Wk 15**	**Wk 24 & Q12wks**		
Window															**±1D**	**±1D**	**±1D**	**±3D**	**±3D**	**±3D**	**±7D**		
Informed consent[a]	X	X																					
Demographics	X																						
HLA-genotyping	X																						
NY-ESO-1 and LAGE-1a levels on BM aspirate	X																						
Inclusions/ Exclusions		X		X																			
Baseline characteristics[e]				X																			
Medical History[f]		X																					
Physical Exam[g]		X		X																	X		
Prior/Concomitant medication[h]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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208470

	Screening[a] Phase / Eligibility Phase		Treatment Phase																			DC of Pembrolizumab Tx[c]	Completion of Treatment Phase or WD[d]
			Leukapheresis	Baseline ≤7 days prior to chemo	Lymphodepleting Chemotherapy[b]					T-cell infusion													
Study Day	**Scrn**	**Elig**		**D -14 to D -8**	**D -8**	**D-7**	**D -6**	**D -5**	**D -4**	**D 1**	**D2**	**D3**	**D4**	**D5**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 6**	**Wk 15**	**Wk 24 & Q12wks**		
Window															**±1D**	**±1D**	**±1D**	**±3D**	**±3D**	**±3D**	**±7D**		
ECOG PS		X		X						X					X	X	X	X	X	X	X	X	X
Vital signs / Weight		X		X						X[i]	X	X	X	X	X	X	X	X	X	X	X	X	X
Pulse oximetry		X		X																			
ECG		X[j]		X[j]						X			X		X								
Echo / MUGA		X[a,k]																					
Chest X-ray (if indicated)		X																					
Hematology		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Clinical Chemistry		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Coagulation tests[l]		X		X																			
Pregnancy test[m]		X		X																			
Urinalysis[l]		X		X																			
Infectious Disease screen[n]		X																					
CMV PCR[o]				X						X					X			X	X				
Thyroid Function Tests[l]				X						X									X then Q6wks (Arm 2 only) →				

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208470

	Screening[a] Phase / Eligibility Phase		Treatment Phase																			DC of Pembrolizumab Tx[c]	Completion of Treatment Phase or WD[d]
			Leukapheresis	Baseline ≤7 days prior to chemo	Lymphodepleting Chemotherapy[b]					T-cell infusion													
Study Day	**Scrn**	**Elig**		**D -14 to D -8**	**D -8**	**D-7**	**D -6**	**D -5**	**D -4**	**D 1**	**D2**	**D3**	**D4**	**D5**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 6**	**Wk 15**	**Wk 24 & Q12wks**		
Window															**±1D**	**±1D**	**±1D**	**±3D**	**±3D**	**±3D**	**±7D**		
C-Reactive Protein[p]				X						X				X			X		X				
Uric acid				X						X													
GFR or 24h urine creatinine[q]		X		X																			
Adverse Events[r]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vector Copies (Persistence for safety)[s]										X										X	X[s]		
VSV-G DNA (RCL) for safety[s]										X										X	X[s]		
Leukapheresis, Lymphodepleting Chemotherapy																							
Leukapheresis[t]			X																				
Fludarabine					X	X	X	X															
Cyclophospha-mide						X	X	X															
G-CSF[u]									X														

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208470

	Screening[a] Phase / Eligibility Phase		Treatment Phase																			DC of Pembrolizumab Tx[c]	Completion of Treatment Phase or WD[d]
			Leukapheresis	Baseline ≤7 days prior to chemo	Lymphodepleting Chemotherapy[b]					T-cell infusion													
Study Day	**Scrn**	**Elig**		**D -14 to D -8**	**D -8**	**D-7**	**D -6**	**D -5**	**D -4**	**D 1**	**D2**	**D3**	**D4**	**D5**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 6**	**Wk 15**	**Wk 24 & Q12wks**		
Window															**±1D**	**±1D**	**±1D**	**±3D**	**±3D**	**±3D**	**±7D**		
Administration of Investigational Products																							
NY-ESO-1^{c259}T infusion										X													
Pembrolizumab (Arm 2 only)[v]																	X then Q3wks up to Wk108 →						
Multiple Myeloma Disease assessments																							
Myeloma markers (labs)[w]		X		X											X		X then Q3wks until Wk24, Q6wks until Wk72, Q12wks thereafter until PD →						X
Bone marrow sample[y, z]		X[x]		X															X	X	X		X
Bone survey[aa]				X																X	X		
Research assessments																							
Pharmaco-genetic - Whole Blood Sample				X[ab]																			

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208470

	Screening[a] Phase / Eligibility Phase		Treatment Phase																			DC of Pem-broli-zumab Tx[c]	Comple-tion of Treatment Phase or WD[d]
			Leukapheresis	Baseline ≤7 days prior to chemo	Lymphodepleting Chemotherapy[b]					T-cell infu-sion													
Study Day	**Scrn**	**Elig**		**D -14 to D -8**	**D -8**	**D-7**	**D -6**	**D -5**	**D -4**	**D 1**	**D2**	**D3**	**D4**	**D5**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 6**	**Wk 15**	**Wk 24 & Q12wks**		
Window															**±1D**	**±1D**	**±1D**	**±3D**	**±3D**	**±3D**	**±7D**		
Bone marrow (bone marrow mononuclear cells)[ac]				X															X	X	X		X
Cell pheno-typing & Functional assays - PBMC				X										X	X	X	X	X	X	X	X	X	X
Vector Copies (Persistence for Research)				X										X	X	X	X	X	X				X
Cytokine analyses & Anti-TCR antibodies[p]				X						X[p]		X		X	X	X	X	X	X[p]	X	X[p]	X	X
cfDNA and exosomes		X		X															X	X	X		X

BM = bone marrow; CBC = complete blood count; CMV = cytomegalovirus; CRP = C-reactive protein; DC = discontinuation; DNA = deoxyribonucleic acid; ECHO = echocardiogram; ECOG = Eastern Cooperative Oncology Group; Elig = Eligibility; G-CSF = granulocyte-colony stimulating factor; HBV = hepatitis B virus; HCV = hepatitis C virus;HLA = human leukocyte antigen; HTLV = human T-lymphotropic virus; IMWG = International Myeloma Working Group; MRI = magnetic resonance imaging; MUGA = multiple-gated acquisition scan; PBMC = peripheral blood mononuclear cell; PET = positron emission tomography; PS = Performance Status; RCL = replication competent lentivirus; Scrn = Screening; Tx = treatment; VSV-G = vesicular stomatitis virus envelope glycoprotein; WD = study withdrawal.

a. Written participant informed consent (and participant assent as applicable) must be obtained prior to performing any protocol procedures. An initial Screening informed consent will have been signed prior to obtaining a blood sample for HLA-testing and bone marrow aspirate for antigen testing. The Treatment informed

consent will be signed prior to all other screening procedures. Note: Information regarding ECHO/MUGA scans, and bone surveys which were performed as standard of care assessments within 4 weeks prior to study consent will be acceptable. Laboratory test performed as standard of care and prior to study consent but within 10 days for leukapheresis will be accepted.

b. Lymphodepleting chemotherapy may only be initiated after the manufactured NY-ESO-1^{c259}T-cell product has been received at the site and the bag(s) have passed inspection by site personnel (see further details in study procedures manual [SPM]).

c. Only for participants enrolled on Arm 2: if participant discontinues from pembrolizumab treatment prior to relapse/progression, this treatment discontinuation visit must be performed including all indicated procedures and assessments listed, unless already recently performed within 30 days. Participant will be maintained in the interventional protocol until disease progression, following the same schedule for safety and disease assessment as Arm 1, and will be transferred to the LTFU protocol ADP-0000-002 as soon as they meet conditions defined under Protocol Section 4.4..

d. If participant withdraws from the treatment phase prior to disease progression, a completion/withdrawal visit must be performed including all procedures and assessments listed indicated, unless already recently performed within 30 days. All participants will be transferred to the LTFU protocol ADP-0000-002 upon completion/withdrawal from treatment phase as soon as they meet conditions defined under Protocol Section 4.4. .

e. Baseline characteristics include recording time from initial diagnosis and time from last therapy.

f. Includes prior lines of therapy.

g. Physical Exam (PE) will only be collected at screening and baseline and every 6 months – any abnormal findings outside these time points will be reported as an AE.

h. Includes concomitant medication since last visit.

i. Vital signs (temperature, pulse, respirations and blood pressure) on the day of T-cell infusion should be taken pre-infusion; and at 5, 15 and 30 minutes, and 1, 1.5, 2, and 4 hours after infusion has started.

j. Cardiac stress test is performed for participants who are 55 years of age or over (specificity of the test will be at Investigator's discretion).

k. MUGA and/or ECHO are required at screening. May also be performed post-lymphodepleting chemotherapy if clinically indicated at the discretion of the Investigator.

l. Additional tests may be performed at any time if clinically indicated.

m. Pregnancy test for Female Participant of Reproductive Potential (FSRP) only.

n. Testing for infectious disease markers is required only at screening and does not need to be repeated at Baseline to satisfy the inclusion / exclusion criteria. Participants who are hepatitis B surface antigen negative but are hepatitis B core antibody positive must have undetectable hepatitis B DNA. Participants who are HCV antibody positive will be screened for HCV RNA by any RT-PCR or bDNA assay.

o. CMV seropositive participants will continue to be monitored at least every 3 weeks for CMV viremia by CMV DNA PCR until 9 weeks post T-cell infusion (Protocol Section 8.2.3)

p. Sample for Cytokine levels at Day 1 will be collected pre-infusion. If cytokine release syndrome (CRS) is suspected, cytokine levels as well C-reactive protein levels should be measured approximately every other day until symptoms are improving or an alternative diagnosis is confirmed. Anti-TCR antibodies will be assessed from the same collection as for Cytokines but only at Baseline, Week 6 and Week 24.

q. Only for participants ≥65 years of age.

r. Refer to Protocol Section 9.1 for instructions and details of AE collection and periods.

s. Vector Copies (Persistence) and VSV-G DNA (RCL) are Central Labs. Vector copies for safety samples are collected Day1 (pre-infusion) and at Week 15, Week 24, and Week 48 post T-cell infusion, then every 6 months post T-cell infusion from year 2-5, and annually from year 6-15. RCL samples are collected Day1 (pre-infusion), and at Week 15, Week 24, and Week 48 post T-cell infusion, and then annually.
t. Testing of participant leukapheresis will meet regional legislative requirements. In the EU this may include screening for Treponema pallidum (syphilis), details will be defined in the SPM.
u. G-CSF will be given from 24 hours after the last dose of cyclophosphamide until resolution of neutropenia in accordance with American Society of Clinical Oncology (ASCO) guidelines or institutional practice. Long-acting (pegylated) G-CSF may be substituted according to institutional practice as described in Protocol Section 8.8.1.
v. Participants in Arm 2 will receive 200 mg pembrolizumab IV for the first time on Week 3 Subsequent doses will be administered every 3 weeks thereafter up to Week 108. Schedule adjustments are outlined in the protocol (Protocol Section 5.4.1).
w. SPEP + immunofixation; quantitative IgG, IgM, IgA; UPEP + immunofixation based on 24 hour urine collection; serum free κ and λ light chain levels and κ/λ ratio determination; beta-2-microgobulin.
x. The BM sample is optional for eligibility if participant had prior histological confirmation of the disease.
y. Bone marrow (BM) sampling should be preferably an aspirate over a fresh biopsy; aspirates are required at Screening, Baseline, as well as for MRD analysis.
z. BM samples will be obtained at baseline, at Week 15 and at Disease Progression (before starting a new treatment) per standard of care and at the time of a complete response assessment (per IMWG response criteria, see Protocol Section 16.4). If the participant received systemic anticancer therapy between leukapheresis and lymphodepleting chemotherapy for disease control, then the timing of the BM sample at baseline is critical and must respect the wash-out periods of Exclusion criterion #3 (Protocol Section 4.2). A BM sample will also be collected at Week 6. A BM sampling at Week 24 is strongly recommended but not mandatory (per PI's discretion). A BM sampling should also be analyzed at the time of a complete response (CR) assessment as per IMWG criteria (see Protocol Section 16.4), in order to confirm CR. Additional BM samples for research purposes semi-annually (optional) or whenever follow-up marrow collection may be performed at PI's discretion. The BM sample obtained at the time point believed to be the closest to maximum response will be analyzed for Minimal Residual Disease (MRD). Refer to Protocol Section 7.5.3 for further specific details.
aa. MRI and PET scan if clinically indicated.
ab. If pharmacogenetics sample collection is not done at baseline, it may be done at any other subsequent visit while the participant is in the treatment phase of the study. Collection of pharmacogenetics sample is optional and all participants who participate must provide consent for pharmacogenetics blood sample collection.
ac. Will be conducted every time a BM sample is obtained. Research includes tumor antigen, gene marked T-cells, T-cell clones and cytokines. Cytogenetics should be performed at least at baseline and at relapse.

14.2.2. Schedule of Procedures in Long-Term Follow-up prior to Transfer to LTFU Protocol

Time post-infusion												
	Year 1			Year 2		Year 3		Year 4		Year 5		Years 6-15
Months	3	6	12	18	24	30	36	42	48	54	60	Annually
Visit window	± 2 weeks		± 3 months									± 6 months
Safety Assessments												
Medical History and Physical Exam[1]		X	X	X	X	X	X	X	X	X	X	X
Mutagenic agents, other investigational agents or anti-cancer therapies[1]		X	X	X	X	X	X	X	X	X	X	X
Adverse Events[2]		X	X	X	X	X	X	X	X	X	X	X
Hematology		X	X		X		X		X		X	X[3]
Serum chemistry		X	X		X		X		X		X	X[3]
Central Lab												
VSV-G DNA (RCL) for safety[4]	X	X	X		X		X		X		X	X
Vector Copies (Persistence) for safety[5]	X	X	X	X	X	X	X	X	X	X	X	X[3]
Other Assessments												
Overall Survival		X	X	X	X	X	X	X	X	X	X	X

1. New medical history/medications/chemotherapies
2. Adverse event collection is limited to:
   - New malignancies
   - New incidence or exacerbation of a pre-existing neurologic disorder
   - New incidence or exacerbation of a prior rheumatologic or other autoimmune disorder
   - New incidence of a hematologic disorder
   - Opportunistic and or serious infections
   - Unanticipated illness and/or hospitalization deemed related to gene modified cell therapy
3. In year 6-15, laboratory assessments are performed for as long as persistence is analyzed. If persistence samples are discontinued (Protocol Section 10.3.1 and Section 10.3.2) then laboratory assessments are discontinued.
4. Samples for RCL (VSV-G copies) are collected as described in Protocol Section 10.1.1.
5. Samples for persistence are collected as described in Protocol Section 10.1.3.1 and Section 10.1.3.2

14.3. Appendix 3: Assessment Windows

14.3.1. Definitions of Assessment Windows for Analyses

No assessment windows will be applied.

14.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

14.4.1. Study Phase

14.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	End date of medication is not missing and is before the start date of lymphodepletion OR lymphodepletion chemotherapy start date is missing
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

14.4.1.2. Study Phases for Anti-Cancer Therapy/Surgery

Study Phase	Definition
On-Study	Start date is on or after the first day of lymphodepletion chemotherapy (both start date and lymphodepletion chemotherapy start date not missing).
Prior	Not classified as On-Study.

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for anti-cancer therapy

The prior phase will be further subdivided as follows:

Study Phase	Definition
Prior to leukapheresis	If classified as prior and entered on the screening visit 2 eCRF
Leukapheresis to lymphodepletion	If classified as prior and not entered on the screening visit 2 eCRF.

NOTES:

- Please refer to Appendix 7 for handling of missing and partial dates for anti-cancer therapy

14.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after lymphodepletion chemotherapy start date. (Lymphodepletion Start Date ≤ AE Start Date) • If AE onset date is missing and AE end date is before the lymphodepletion start date, then the AE will not be classified as Treatment-Emergent. If AE onset date is missing and AE end date is either missing or on or after lymphodepletion start date, then the AE will be classified as treatment-emergent • Partially missing AE onset and end dates will be imputed following rules in Section 14.7.2.1 for determining Treatment Emergent AEs

14.5. Appendix 5: Data Display Standards & Handling Conventions

14.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: US1SALX00259
HARP Compound	: arprod\GSK3377794\mid208470
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1).	
Generation of RTF Files	
• RTF files will be generated for SAC.	

14.5.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings
• While text within this RAP uses the term “participant”, all data displays (Tables, Figures, and Listings) will use the term “subject”, reflecting CDISC and GSK Data Display Standards terminology.

Formats
• GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP’s) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP’s.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant’s listings.

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables and/or figures, except in cases where worse-case post-baseline is calculation. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

14.5.3. Reporting Standards for Pharmacokinetic Data

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	All PK parameters will be derived by the PK programmer. No WNL file will be produced.
ADPC data file	Persistence data will be captured in ADBIOMRK, and derived persistence parameters will be captured as additional PARAMCD values in ADBIOMRK. No ADPC data file will be created.
Descriptive Summary Statistics, Graphical Displays and Listings	Example shells for persistence are provided in Appendix 13. Refer to IDSL Statistical Principle 6.06.1. **Note:** Concentration values will be imputed as per rules in the RAP.
Pharmacokinetic Parameter Derivation	
PK Parameters to be Derived by PK Programmer	The following PK parameters will be derived by the PK Programmer: Cmax, Tmax, and $AUC_{(0-28)}$.
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	No.

14.6. Appendix 6: Derived and Transformed Data

14.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • For character variables, if multiple assessments on different days are reported for the same scheduled assessment, then the worst-case assessment for that scheduled assessment will be analysed. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from T-cell infusion date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < T-cell infusion Date → Study Day = Ref Date – T-cell infusion Date
  • Ref Date ≥ T-cell infusion Date→ Study Day = (Ref Date – T-cell infusion Date) + 1

Change from Baseline
• Change from Baseline = Post-Baseline Visit Value – Baseline • % Change from Baseline = 100 x (Post-Baseline Visit Value – Baseline) / Baseline • Maximum Increase/Decrease from Baseline = maximum (Increase/Decrease from Baseline) • If either the Baseline or Post-Baseline Visit Value is missing, then both Change from Baseline and % Change from Baseline are set to missing
Date of New on Study Anti-Cancer Therapy
• Derived as the earliest date of new systemic anti-cancer therapy • Missing or partial dates will be imputed for derivation of new anti-cancer therapy following rules specified in Section 14.7.2.1.

14.6.2. Study Population

Age
• For participants with a T-cell infusion date, age is derived using T-cell infusion date as the reference date. For ITT participants without a T-cell Infusion date, date of eligibility for apheresis is used as the reference date.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)^2]**
Time since Initial Diagnosis to Screening ICF signed
• Time (in months) since initial diagnosis to screening will be calculated below: • Months since initial diagnosis = (Date of Screening Visit (Screening ICF Signed) - Date of Initial diagnosis +1) / 30.4375

On-study Treatment Follow-up Time
• Time (in months) from T-cell infusion to end of follow-up will be calculated below: • Months of on-study treatment follow-up = (Date of Death/Last Contact – T-cell Infusion Date+1) / 30.4375
Extent of Exposure (Pembrolizumab)
• Number of days of exposure to Pembrolizumab will be calculated based on the formula: **Duration on study treatment** is calculated as the minimum of: ◦ Last treatment stop date – first treatment start date + 21 ◦ Date of death – first treatment start date + 1 • Participants who did not report a Pembrolizumab start date will be categorised as having zero days of exposure. • The cumulative actual dose in mg for Pembrolizumab will be based on the formula: **Cumulative Dose (mg) = Sum of (200 mg * % of bag infused at each visit)** • Dose intensity (mg/per 3 weeks) for Pembrolizumab is the cumulative actual dose divided by expected duration of exposure in 3 weeks (expected = (last infusion date – first infusion date + 21)/21)

14.6.3. Safety

Adverse Events
Adverse Events of Special Interest (AESIs)
The events of special interest included from protocol Section 9.13 (Adverse Events of Special Interest). This section includes the following events: • Guillain-Barre Syndrome • Recurrent Pancytopenia/Aplastic Anaemia • Immune Effector-Cell Associated Neurotoxicity Syndrome (ICANS) • Graft versus Host Disease (GVHD) • Cytokine Release Syndrome (CRS)
Duration of AE
• Calculated as the number of days from AE Start Date to AE Stop Date: ◦ AE Start Date = Missing → Elapse Time = Missing ◦ AE Stop Date = Missing → Elapse Time = Missing Otherwise → Elapsed Time = AE Stop Date – AE Start Date + 1 Imputed dates will not be used to calculate AE duration.

Laboratory Parameters
• If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the following rules will be applied to impute numeric values: ◦ If the reported value is "NOT DETECTED" (or some other indicator of such), then impute to 0 (zero). ◦ If the reported value is "OLIGOCLONAL POP" (or some other indicator of such), then no imputation of a numeric value will be applied. ◦ If the reported value is "TRACE" (or some other indicator of such), then no imputation of a numeric value will be applied.

14.6.4. Efficacy

Refer to Section 7 for endpoint derivation information.

Secondary Endpoints
Date of Last Contact
• Last date in all SDTM domains • If patient died, the last contact date should be death date. • Dates after date of death will be excluded. Future dates will be excluded. • SDTM domain SE will be excluded and SDTM variables DM.BRTHDTC, MH.MHSTDTC, SV.SVENDTC, SV.SVSTDTC, DM.RFPENDTC, _ALL_.ANALDTC, DV.DVDTC, DV.DVSTDTC, and any other external source data dates as necessary will be excluded • Partial and missing dates will not be imputed for the purpose of deriving date of last contact

14.7. Appendix 7: Reporting Standards for Missing Data

14.7.1. Premature Withdrawals

Element	Reporting Detail
General	• A participant will be considered to have completed the treatment phase (as specified in the protocol) at the earliest point of confirmed progressive disease, 108 weeks following NY-ESO-1^{c259}T-cell infusion, or death. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

14.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
Responder Analysis	• For endpoints which determine the percentage of responders, participants with unknown/not evaluable or missing best overall response will be assumed to be non-responders and will be included in the denominator when calculating the percentages.

14.7.2.1. Handling of Missing and Partial Dates

Imputed partial dates can be used to derive study day, duration, or elapsed time variables, unless otherwise specified. However, imputed dates are not used for deriving the last contact date in the overall survival analysis dataset.

Imputed dates will not be displayed in listings. For listings, use the SDTM character date variables and do not show day and duration based on imputed dates. The imputed dates can be used for sorting the data for listings. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes, as outlined below.

The partial date imputation will follow ADaM conventions. The ADaM approach is to populate the numeric date variables with the imputed date and add a flag variable to the dataset that indicates the level of imputation.

The flag variable can contain the values: blank, 'D', 'M', 'Y'.

blank: indicates that no imputation was done

D='Day': indicates that the day portion of the date is imputed

M='Month': indicates that the month and day portions of the date are imputed

Y='Year': indicates that the entire date (year, month, and day) is imputed

Example of date variables:

XYZDTC_ − character date variable

XYZDT − numeric date variable

XYZDTFL − flag variable

Details on imputing partial dates for specific datasets are outlined below.

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td>General</td><td>• Partial dates will be displayed as captured in participant listing displays.</td></tr>
<tr><td>Adverse Events</td><td>• Imputations in the adverse events dataset are used for slotting events to the appropriate study time periods and for sorting in data listings.
• Partial dates for AE recorded in the eCRF will be imputed using the following conventions:
<table>
<tr><td>Missing start day</td><td>• If lymphodepletion start date is missing (i.e. participant did not start lymphodepletion), then set start date = 1st of month.
• Else if lymphodepletion start date is not missing:
o If month and year of start date = month and year of lymphodepletion start date then
▪ If stop date contains a full date and stop date is earlier than lymphodepletion start date then set start date= 1st of month.
▪ Else set start date = lymphodepletion start date.
o Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If lymphodepletion start date is missing (i.e. participant did not start lymphodepletion), then set start date = January 1st.
• Else if lymphodepletion start date is not missing:
o If year of start date = year of lymphodepletion start date then
▪ If stop date contains a full date and stop date is earlier than lymphodepletion start date then set start date = January 1st.
▪ Else set start date = lymphodepletion start date.
o Else set start date = January 1st.</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table></td></tr>
<tr><td>Anti-Cancer Therapy (including</td><td>• Completely missing start or end dates will remain missing, with no imputation applied.
• If partial start date contains a year only set to January 1st.</td></tr>
</table>

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td>stem cell transplant) and Radiotherapy</td><td>• If partial start date contains a month and year set to the 1st of the month.
• Partial or missing end dates will not be imputed.</td></tr>
<tr><td>Concomitant Medications/ Blood Supportive Products</td><td>• These imputation rules will be used for classifying a medication as prior or concomitant.
• Completely missing start dates will not be imputed.
• Partial start dates for any concomitant medications recorded in the eCRF will be imputed using the following convention:
<table>
<tr><td>Missing start day</td><td>• If lymphodepletion start date is missing (i.e. participant did not start lymphodepletion), then set start date = 1st of month.
• Else if lymphodepletion start date is not missing:
o If month and year of start date = month and year of lymphodepletion start date then
▪ If stop date contains a full date and stop date is earlier than lymphodepletion start date then set start date= 1st of month.
▪ Else set start date = lymphodepletion start date.
o Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If lymphodepletion start date is missing (i.e. participant did not start lymphodepletion), then set start date = January 1st.
• Else if lymphodepletion start date is not missing:
o If year of start date = year of lymphodepletion start date then
▪ If stop date contains a full date and stop date is earlier than lymphodepletion start date then set start date = January 1st.
▪ Else set start date = lymphodepletion start date.
• Else set start date = January 1st.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table></td></tr>
<tr><td>New Anti-Cancer Therapy/ Stem cell transplants for Efficacy Evaluation (e.g., response rate, time to event)</td><td>• Completely missing start dates will remain missing, with no imputation applied;
• Partial start dates will be imputed using the following convention:
• If both month and day are missing, no imputation will be applied;
• If only day is missing:
o If the month of partial date is the same as the month of T-cell infusion, minimum of (date of T-cell infusion date + 1, last day of the month) will be used for the day;
o If the month of partial date is the same as the month of last disease assessment and the last disease assessment is PD, minimum of (last date of disease assessment + 1, last day of the month) will be used for the day;
o If both conditions above are met, the later date will be used for the day;
o Otherwise, a ‘01’ will be used for the day;
• Completely or partial missing end dates will remain missing, with no imputation applied;</td></tr>
</table>

14.8. Appendix 8: Values of Potential Clinical Importance

14.8.1. Laboratory Values

Reference ranges for all laboratory parameters collected throughout the study are provided by the laboratory. A laboratory value that is outside the reference range is considered either high abnormal (value above the upper limit of the reference range) or low abnormal (value below the lower limit of the reference range). Note: a high abnormal or low abnormal laboratory value is not necessarily of clinical concern. The laboratory reference ranges will be provided on the listings of laboratory data. Clinical laboratory test results outside of the reference range will be flagged in the listings.

To identify laboratory values of potential clinical importance, National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v4.03) will be used to assign grades to the relevant laboratory parameters. NCI-CTCAE v4.03 can be found at http://ctep.cancer.gov/reporting/ctc.html.

For laboratory data which are not listed in the NCI CTCAE v4.03, a summary of values outside the normal range will be provided.

For lab test values that can be graded, values of grade 1 or above are defined as values of potential clinical concern. For lab test values that cannot be graded, values out of the normal range are defined as values of potential clinical concern. For lab tests reported descriptively as 'Normal', 'Abnormal, not clinically significant', or 'Abnormal, clinically significant' (such as urinalysis), responses of 'Abnormal, clinically significant' will be considered as of potential clinical concern.

14.8.2. ECG

The following criteria will be used to flag electrocardiogram (ECG) values that are values of potential clinical importance:

To identify QTc (Bazett's or Fridericia's) values of potential clinical importance, NCI-CTCAE v4.03 will be used to assign grades (see adverse event 'Electrocardiogram QT corrected interval prolonged'). The eCRF collects either QTcB or QTcF. Note that there is a slight inconsistency between CTCAE v4 and ICH E14 (Absolute QTc interval prolongation). It was decided to align with CTCAE for the oncology standard categories.

The following criteria will be used to flag other ECG values that are values of potential clinical importance:

PCI Flag	Potential Clinical Importance (PCI) Range	Unit
High (H)	Grade 2 or Higher (QTc≥481) or QTc increase from baseline of >30msec	Msec

14.8.3. Vital Signs

To identify heart rate values of potential clinical importance, NCI-CTCAE v4.03 will be used to assign categories that align with the grades for 'Sinus bradycardia', 'Sinus tachycardia', 'Supraventricular tachycardia', and 'Ventricular tachycardia'.

The following criteria will be used to flag vital sign values that are values of potential clinical importance:

Vital Sign Parameter	Potential Clinical Importance (PCI) Range	Unit
Decrease from baseline Heart Rate	Decrease to <60	bpm
Increase from baseline Heart Rate	Increase to >100	bpm

To identify blood pressure values of potential clinical importance, NCI-CTCAE v4.03 will be used to assign categories that align with the grades for 'Hypertension'.

Vital Sign Parameter	Potential Clinical Importance (PCI) Range	Unit
Increase from baseline Systolic Blood Pressure	≥120 to <140 (Grade 1) ≥140 to <160 (Grade 2) ≥160 (Grade 3)	mmHg
Increase from baseline Diastolic Blood Pressure	≥80 to <90 (Grade 1) ≥90 to <100 (Grade 2) ≥100 (Grade 3)	mmHg

To identify temperature values of potential clinical importance, NCI-CTCAE v4.03 will be used to assign categories that align with the grades for 'Hypothermia' and 'Fever'.

Vital Sign Parameter	Potential Clinical Importance (PCI) Range	Unit
Increase from baseline temperature	Increase to ≥38	Degrees C
Decrease from baseline temperature	Decrease to ≤35	Degrees C

To identify respiratory rate of potential clinical importance, NCI-CTCAE v4.03 will be used to assign categories that align with the grades for 'Respiratory'.

Vital Sign Parameter	Potential Clinical Importance (PCI) Range	Unit
Increase from baseline respiratory rate	Increase to >30	Breaths/minute

14.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

Not applicable.

14.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

Not applicable.

14.11. Appendix 11: Abbreviations & Trademarks

14.11.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Curve
BMMC	Bone Marrow Mononuclear Cells
BOR	Best Overall Response
CDISC	Clinical Data Interchange Standards Consortium
Cmax	Peak Expansion
CMV	Cytomegalovirus
CPMS	Clinical Pharmacology Modelling & Simulation
CR	Complete Response
CRP	C-reactive Protein
CRS	Cytokine Release Syndrome
CSR	Clinical Study Report
CTCAE	Common Toxicity Criteria for Adverse Events
DNA	Deoxyribonucleic Acid
DBF	Database Freeze
DBR	Database Release
DoR	Duration of Response
DP	Decimal Places
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Record Form
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FLC	Free Light Chain
GBS	Guillain-Barre Syndrome
G-CSF	Granulocyte-Colony Stimulating Factor
GSK	GlaxoSmithKline
GvHD	Graft versus Host Disease
HLA	Human Leukocyte Antigen
IA	Interim Analysis
ICANS	Immune Effector-Cell Associated Neurotoxicity Syndrome
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
IMWG	International Myeloma Working Group
IP	Investigational Product
ITT	Intent-To-Treat
LFT	Liver Function Test

Abbreviation	Description
LTFU	Long-Term Follow-Up
mITT	Modified Intent-To-Treat
MR	Minimal Response
MRD	Minimal Residual Disease
NCI	National Cancer Institute
NE	Not Evaluable
ORR	Overall Response Rate
OS	Overall Survival
PCI	Potential Clinical Importance
PCR	Polymerase Chain Reaction
PD	Progression Disease
PFS	Progression-free Survival
PP	Predictive Probability
PR	Partial Response
PT	Preferred Term
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RCL	Replication Competent Lentivirus
RRMM	Relapsed Refractory Multiple Myeloma
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
sCR	Stringent Complete Response
SD	Stable Disease
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SRT	Safety Review Team
TFL	Tables, Figures & Listings
TLT	Treatment Limiting Toxicity
Tmax	Time to Peak Expansion
TTR	Time to Response
ULN	Upper Limit of Normal
VGPR	Very Good Partial Response

14.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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14.12. Appendix 12: List of Data Displays

14.12.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.0010 to 1.0220	NA
Efficacy	2.0010 to 2.0020	2.0030 to 2.0070
Safety	3.0010 to 3.0620	3.0630 to 3.0680
Biomarker	3.0690 to 3.0690	NA
Pharmacokinetic	4.0010 to 4.0020	4.0030 to 4.0050
Section	**Listings**	
ICH Listings	0010 to 0430	
Other Listings	0440 to 0520	

14.12.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 13: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Biomarker	BIO_Fn	BIO_Tn	BIO_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

14.12.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

14.12.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.0010	mITT	[Non-Standard] POP_T2	Summary of Subject Status – Treatment Phase (mITT)	ICH E3, FDAAA, EudraCT Subject Status: Completed, Ongoing, Did not complete. Use reasons on the EOT CRF (reason for early discontinuation) for withdrawal, prepopulate all of them in the display. Note that progressive disease, death, and not progressed at 108 weeks are the only reasons for completion of the treatment phase. Not aligned w/study 208469 (MRCLS).	SAC
1.0020	mITT	[Non-Standard] POP_T3	Summary of Subject Status – End of Study (mITT)	ICH E3, FDAAA, EudraCT Use logic provided in RAP text to derive end-of-study status. Subject Status: Completed, Ongoing, Withdrawn Reason for withdrawal comes from treatment phase table above. Not aligned w/study 208469 (MRCLS).	SAC
1.0030	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements Align w/study 208469 (MRCLS).	SAC
1.0040	ITT	SD4	Summary of Reasons for Study Treatment Discontinuation (Pembrolizumab)	Only include participants from Arm 2. Reasons for discontinuation should match the Pembrolizumab disposition eCRF in content and order Not aligned w/ 208469 (MRCLS)	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0050	Enrolled	NS1	Summary of Number of Subjects by Country and Site ID	EudraCT/Clinical Operations Align w/study 208469 (MRCLS).	SAC
Population Analysed					
1.0060	Screened	SP1A	Summary of Study Populations	IDSL Screened, Enrolled, ITT, mITT only. Align w/study 208469 (MRCLS).	SAC
Protocol Deviations					
1.0070	ITT	DV1	Summary of Important Protocol Deviations	ICH E3 Align w/study 208469 (MRCLS).	SAC
Demographic and Baseline Characteristics					
1.0080	mITT	DM1	Summary of Demographic Characteristics (mITT)	ICH E3, FDAAA, EudraCT Report baseline height, weight, BMI, and BSA. Report Race but not Race Detail. Age groups to be presented: <=18, 19-64, and >=65 years. Align w/study 208469 (MRCLS).	SAC
1.0090	Enrolled	DM11	Summary of Age Ranges	EudraCT Age groups to be presented: 18-64, 65-84 and >=85 years. Align w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Disease Characteristics					
1.0100	mITT	DC1	Summary of Disease Characteristics at Initial Diagnosis (mITT)	ICH E3 Time from initial diagnosis to screening ICF signed (in months), stage at diagnosis, histologic type, % clonal bone marrow plasma cells, presence and type of end organ damage, presence and type of plasmacytoma, and chromosomal aberrations (previously referred to as karyotype). Not aligned w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0110	mITT	DC2	Summary of Disease Characteristics at Screening (mITT)	ICH E3 Type of multiple myeloma (IgA Kappa, IgA Lambda, IgG Kappa, etc.), HLA status (Allele 1 & Allele 2), NY-ESO-1 status, LAGE-1a status, number of radiotherapy regimens prior to leukapheresis, number of systemic therapy regimens prior to leukapheresis, receipt of stem-cell transplant prior to leukapheresis (Y/N), bone lesion (Y/N), and subtype of stem-cell transplant received (autologous or allogeneic). Break down "Number of Prior Systemic Therapy Regimens" into {0,1,2,3,4,5,6,>6}. Also, use the new derivation of lines of systemic therapy (i.e., count systemic therapy + conditioning chemo associated w/stem cell therapy) – please add a footnote that makes this clear. Not aligned w/study 208469 (MRCLS).	SAC
Medical Conditions and Concomitant Medications					
1.0120	mITT	MH4	Summary of Medical Conditions (mITT)	ICH E3 Include both past and ongoing medical conditions at screening. Align w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0130	mITT	CM8	Summary of Concomitant Medications (mITT)	ICH E3 Use GSK Drug Coding Dictionary Align w/study 208469 (MRCLS).	SAC
1.0140	mITT	BP1A	Summary of Blood Products on Treatment (mITT)	Using the same rule as con meds, include only "concomitant blood products" in the display and provide a footnote that explains this clearly. Align w/study 208469 (MRCLS).	SAC
Anti-Cancer Therapy					
1.0150	mITT	AC1	Summary of Prior Anti-Cancer Therapy (mITT)	IDSL In addition to prior systemic and radiation therapies, please include prior stem cell therapy (by subtype: autologous or allogeneic) in this summary. Systemic therapy should include prior to leukapheresis + full line of therapy starting after leukapheresis, and radiotherapy and surgery should include prior to lymphodepletion. Add footnote: “Note: Includes all anti-cancer therapy prior to lymphodepletion except bridging therapies.” With the exception of stem cell being included, this display should align w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0160	mITT	FAC1	Summary of On-Study Anti-Cancer Therapy (mITT)	IDSL Add time from T-cell infusion to the first post-treatment anti-cancer therapy. In addition to systemic and radiation therapies, please include stem cell therapy (by subtype: autologous or allogeneic) in this summary. With the exception of stem cell being included, this display should align w/study 208469 (MRCLS).	SAC
1.0170	mITT	CM1	Summary of Prior Dictionary Coded Anti-Cancer Therapy (mITT)	IDSL Use GSK Drug Coding Dictionary Systemic therapy should include prior to leukapheresis + full line of therapy starting after leukapheresis, and radiotherapy should include prior to lymphodepletion. Note that while stem cell therapy is not included in this summary, conditioning chemotherapy for the stem cell therapy is included. Add footnote: “Note: Includes all anti-cancer therapy prior to lymphodepletion except bridging therapies.” Add footnote: “Note: Stem cell therapy is not included in this summary.” Align w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0180	mITT	AC3	Summary of Number of Prior Anti-Cancer Therapy Regimens (mITT)	IDSL Summarize all prior systemic therapy and radiotherapy regimens prior to lymphodepletion. Do not split out by type of systemic regimen as multiple types could make up a regimen. Add footnote: "Note: Includes all anti-cancer therapy prior to lymphodepletion except bridging therapies." Not aligned w/study 208469 (MRCLS)	SAC
1.0190	mITT	CM1	Summary of On-Study Dictionary Coded Anti-Cancer Therapy (mITT)	IDSL Use GSK Drug Coding Dictionary Note that while stem cell therapy is not included in this summary, conditioning chemotherapy for the stem cell therapy should be included. Add footnote: "Note: Stem cell therapy is not included in this summary." Align w/study 208469 (MRCLS).	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.0200	mITT	CM1	Summary of Bridging Therapy (mITT)	IDSL Summarize all prior therapies identified as bridging. In addition to systemic and radiation therapies, please include prior stem cell therapy in this summary. With the exception of stem cell being included, this display should align w/study 208469 (MRCLS). Add footnote: "Note: Includes all anti-cancer therapy initiated between leukapheresis and lymphodepletion identified as bridging."	SAC
Exposure					
1.0210	mITT	OEX1	Summary of Total Infused Transduced T-cells	Report total number of infused transduced T-cells in 10^9 cells and categorize it into: <1, >=1 to <=8, >8 and <1, >=1 to <=3, >3 to <=8, >8 Align w/study 208469 (MRCLS).	SAC
1.0220	mITT	[Non-Standard] POP_T1	Summary of Leukapheresis, Lymphodepletion, T-cell Infusion, and Pembrolizumab Administration	Add number of subjects infused with minimum dose of 1 x 10^9 transduced cells (i.e., in addition to the total number who underwent infusion). Please add a line for Pembro. Not aligned w/study 208469 (MRCLS).	SAC

14.12.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Overall Response Rate (ORR)					
2.0010	mITT	RE1a	Summary of Investigator-Assessed Best Response with Confirmation (IMWG 2016) (mITT)	Add Total column. Add Overall Response (sCR + CR + VGPR + PR) and include 95% CI for Overall Response Rate. Omit all hypothesis testing sections. Not aligned w/study 208469 (MRCLS).	SAC
Time to Event					
2.0020	mITT	TTE1	Summary of Investigator-Assessed Progression Free Survival (IMWG 2016)	Unit = months. Include a Total column. Only create if at least 3 subjects in the study Omit all hypothesis testing sections i.e., Hazard Ratio estimate and 95%CI (marked as optional in IDSL shell). Include footnote: "Note: Progression Free Survival is defined as the interval between the date of T-cell infusion and the date of confirmed progressive disease or death per IMWG 2016." Align w/study 208469 (MRCLS).	SAC

14.12.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Responses by Myeloma Biomarkers					
2.0030	mITT	[Non-Standard] EFF_F1	Percent Change at Maximum Reduction from Baseline in M-Protein or Serum Free Light Chain (FLC) Measurement	Waterfall plot. Use Serum M-protein, Urine-M-protein (if no Serum M-protein) and difference between 2 types of Serum FLC (if Serum M-protein and Urine M-protein not available), as relevant per subject. Do not report separately by arm; rather, include all subjects on the same plot. Color the bars by "Type of Myeloma Marker" and "Treatment Arm". Example: Arm 1 Serum M prot='Solid Blue', Arm 2 Serum M prot='Striped Blue'. Not aligned w/study 208469 (MRCLS).	SAC
2.0040	mITT	[Non-Standard] EFF_F2	Spider Plot of Percent Change from Baseline in Myeloma Biomarkers by Subject	Create a separate plot for each subject, showing on each plot: Serum M-protein, Urine-M-protein and difference between 2 types of Serum FLC. Include date of first pembro dose on the plot for each subject. Not aligned w/study 208469 (MRCLS).	SAC
2.0050	mITT	[Non-Standard] EFF_F2	Composite Spider Plot of Percent Change from Baseline in Myeloma Biomarkers for All Subjects	Create a composite plot, with all subjects included (1 line per subject). The line for each subject will represent the subject's "chosen marker" from the waterfall plot above. Include date of first pembro dose on the plot for each subject.	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Not aligned w/study 208469 (MRCLS).	
Time to Event					
2.0060	mITT	TTE10	Graph of Kaplan-Meier Curve of Investigator-Assessed Progression Free Survival with 95% Confidence Band by Treatment Arm (IMWG 2016)	Unit = months. Create separate KM curves (lines) for treatment arms (distinguish lines by color or pattern). Only create if at least 3 subjects in a single arm. Similar to the footnote used in DoR displays, add a footnote that defines PFS as including confirmed progressive disease. Align w/study 208469 (MRCLS).	SAC
2.0070	mITT	TTE10	Graph of Kaplan-Meier Curve of Investigator-Assessed Progression Free Survival with 95% Confidence Band for All Subjects (IMWG 2016)	Unit = months. Create single KM curve for all subjects. Only create if at least 3 subjects overall in the study. Similar to the footnote used in DoR displays, add a footnote that defines PFS as including confirmed progressive disease. Align w/study 208469 (MRCLS).	SAC

14.12.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (AEs)					
3.0010	ITT	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3 Add Total column. Do not use combined PTs. Align w/study 208469 (MRCLS).	SAC
3.0020	mITT	AE1	Summary of All Treatment Emergent Adverse Events by System Organ Class and Preferred Term	ICH E3 Add Total column. Do not use combined PTs. Treatment emergent only. Align w/study 208469 (MRCLS).	SAC
3.0030	ITT	OAE07	Summary of All Adverse Events by Maximum Grade Separately for Treatment Arms and Overall	Add total "by group" page (i.e., subheading should be “Treatment: Total (N=XXX)”). Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0040	ITT	AE18	Summary of All Adverse Events by Maximum Grade and Treatment Arm	Include Total column. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.0050	mITT	OAE07	Summary of All Treatment Emergent Adverse Events by Maximum Grade Separately for Treatment Arms and Overall	Treatment emergent only. Add total "by group" page (i.e., subheading should be “Treatment: Total (N=XXX)”). Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0060	mITT	AE18	Summary of All Treatment Emergent Adverse Events by Maximum Grade and Treatment Arm	Treatment emergent only. Include Total column. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	SAC
3.0070	mITT	OAE07	Summary of All Study-Treatment Related Adverse Events by Maximum Grade Separately for Treatment Arms and Overall	ICH E3 Treatment emergent only. Add total by-group page. Treatment related, including lymphodepleting chemotherapy, T-cell infusion, and pembrolizumab. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.0080	mITT	AE18	Summary of All Study-Treatment Related Adverse Events by Maximum Grade and Treatment Arm	ICH E3 Treatment emergent only. Include Total column. Treatment related, including lymphodepleting chemotherapy, T-cell infusion, and pembrolizumab. Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	SAC
3.0090	mITT	OAE07	Summary of All T-Cell Infusion Related Adverse Events by Maximum Grade Separately for Treatment Arm and Overall	ICH E3 Treatment emergent only. Add total by-group page. Treatment related (T-cell infusion). Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0100	mITT	AE18	Summary of All T-Cell Infusion Related Adverse Events by Maximum Grade and Treatment Arm	ICH E3 Treatment emergent only. Include Total column. Treatment related (T-cell infusion). Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as column header.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	
3.0110	mITT	OAE07	Summary of All Lymphodepletion-Related Adverse Events by Maximum Grade Separately for Treatment Arm and Overall	ICH E3 Treatment emergent only. Add total by-group page. Treatment related (lymphodepleting chemotherapy). Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0120	mITT	AE18	Summary of All Lymphodepletion-Related Adverse Events by Maximum Grade and Treatment Arm	ICH E3 Treatment emergent only. Include Total column. Treatment related (lymphodepleting chemotherapy). Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	SAC
3.0130	ITT	OAE07	Summary of All Serious Adverse Events by Maximum Grade Separately for Treatment Arm and Overall	ICH E3 Treatment emergent only. Serious events. Add total by-group page. Use combined PTs with footnote "Preferred terms are combined."	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	
3.0140	ITT	AE18	Summary of All Serious Adverse Events by Maximum Grade and Treatment Arm	ICH E3 Treatment emergent only. Serious events. Include Total column. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as column header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4.	SAC
3.0150	ITT	AE15	Summary of All Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Add Total column. Do not combine Preferred Terms. Align w/study 208469 (MRCLS).	SAC
3.0160	ITT	AE3	Summary of All Non-Serious Study-Treatment Related AEs by Overall Frequency	Add Total column. Do not combine Preferred Terms. Align w/study 208469 (MRCLS).	SAC
3.0170	ITT	AE1	Summary of Adverse Events Grouped by Similarity of Preferred Terms	Add Total column. Use combined PTs with footnote “Preferred terms are combined.” Remove overall “ANY EVENT” and synonym level “Any Event” rows. SOC from AE1 should be combined PT. PT from AE1 should be the MEDDRA PT.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Label column "Synonym/Preferred Term" rather than "System Organ Class/Preferred Term" (where / indicates new line and indent as in AE1). If combined AE does not appear then include a 0 count. Align w/study 208469 (MRCLS).	
Adverse Events of Special Interest (AE of SI)					
3.0180	mITT	OAE01	Summary of Treatment Emergent Adverse Events of Special Interest by Maximum Grade (Focused List)	Treatment emergent only. Add total by-group page (i.e., subheading should be "Treatment: Total (N=XXX)"). Use combined PT identified in the focused list with footnote "Preferred terms are combined". Use "Adverse Event" (rather than "Preferred Term") as column header. Replace SOC with AESI category (use AESI category names from current SRT AESI specification document if these differ to those in RAP). Align w/study 208469 (MRCLS).	SAC
3.0190	mITT	OAE01	Summary of Treatment Emergent Adverse Events of Special Interest by Maximum Grade (Comprehensive List)	Treatment emergent only. Add total by-group page (i.e., subheading should be "Treatment: Total (N=XXX)"). Do not use combined PTs.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Replace SOC with AESI category (use AESI category names from current SRT AESI specification document if these differ to those in RAP). Align w/study 208469 (MRCLS).	
3.0200	mITT	ESI1	Summary of Characteristics of Haematopoietic Cytopenias (Focused List)	Treatment emergent only. Add total column. Use Focused Scope List. Footnote – "Preferred terms identified in the Focused list are summarized". Report for all subjects and for all subjects with event. Report characteristics, outcome, number of occurrences and max grade. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC
3.0210	mITT	ESI1	Summary of Characteristics of Cytokine Release Syndrome (CRS)	Treatment emergent only. Add total column. Use Focused Scope List. Footnote – "Preferred terms identified in the Focused list are summarized". Report for all subjects and for all subjects with event. Report characteristics, outcome, number of occurrences and max grade. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC
3.0220	mITT	ESI2a	Summary of Onset and Duration of the First Occurrence of Haematopoietic Cytopenias (Focused List)	Treatment emergent only. Add total column. Use Focused Scope List.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Footnote – "Preferred terms identified in the Focused list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30,31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS). Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	
3.0230	mITT	ESI2a	Summary of Onset and Duration of the First Occurrence of Haematopoietic Cytopenias (Neutropenia)	Treatment emergent only. Add total column. Use Focused Scope Neutropenia List. Footnote – "Preferred terms identified in the Focused neutropenia list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30,31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS). Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	SAC
3.0240	mITT	ESI2a	Summary of Onset and Duration of the First Occurrence of Haematopoietic Cytopenias (Thrombocytopenia)	Treatment emergent only. Add total column.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Use Focused Scope Thrombocytopenia List. Footnote – "Preferred terms identified in the Focused Thrombocytopenia list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30,31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS). Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	
3.0250	mITT	ESI2a	Summary of Onset and Duration of the First Occurrence of Haematopoietic Cytopenias (Anemia)	Treatment emergent only. Add total column. Use Focused Scope Anemia List. Footnote – "Preferred terms identified in the Focused Anemia list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30,31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS). Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.0260	mITT	ESI2a	Summary of Onset and Duration of the First Occurrence of Cytokine Release Syndrome (CRS)	Treatment emergent only. Add total column. Use Focused Scope List. Footnote – "Preferred terms identified in the Focused list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30, 31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS). Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	SAC
3.0270	mITT	ESI2a	Summary of Onset and Duration of the Last Occurrence of Haematopoietic Cytopenias (Focused List)	Treatment emergent only. Add total column. Use Focused Scope List. Footnote – "Preferred terms identified in the Focused list are summarized". Time to onset (days) (-8 - -1, 1 -14, 15-30, 31-60, >60). Remove subjects at risk. Duration (days) (1-30 31-90, >90). Onset from first T-cell infusion. Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Important: The AE collapsing rules of MRCLS should be used for all onset/duration tables, where applicable.	
3.0280	mITT	[Non-Standard] SAFE_T1	Summary of Time to Resolution and Recurrence of Grade 3 and Above Haematopoietic Cytopenias (Focused List)	Treatment emergent only. Use Focused Scope List. Footnote – "Preferred terms identified in the Focused list are summarized". Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC
3.0290	mITT	[Non-Standard] SAFE_T1	Summary of Time to Resolution and Recurrence of Grade 3 and Above Haematopoietic Cytopenias (Neutropenia)	Treatment emergent only. Use Comprehensive Scope List. Footnote – "Preferred terms identified in the Neutropenia focused list are summarized". Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC
3.0300	mITT	[Non-Standard] SAFE_T1	Summary of Time to Resolution and Recurrence of Grade 3 and Above Haematopoietic Cytopenias (Thrombocytopenia)	Treatment emergent only. Use Comprehensive Scope List. Footnote – "Preferred terms identified in the thrombocytopenia focused list are summarized". Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	SAC
3.0310	mITT	[Non-Standard] SAFE_T1	Summary of Time to Resolution and Recurrence of Grade 3 and Above Haematopoietic Cytopenias (Anemia)	Treatment emergent only. Use Comprehensive Scope List. Footnote – "Preferred terms identified in the Anemia focused list are summarized".	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Do not create if 1 or fewer subjects have event (default to listing). Align w/study 208469 (MRCLS).	
Serious and Other Significant Adverse Events					
3.0320	ITT	AE16	Summary of All Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Add Total column. Do not use combined PTs. Align w/study 208469 (MRCLS).	SAC
3.0330	ITT	OAE07	Summary of All Serious Adverse Events by Maximum Grade	Add total "by group" page. Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0340	mITT	OAE07	Summary of All Serious Treatment Emergent Adverse Events by Maximum Grade Separately for Treatment Arm and Overall	Treatment emergent only. Add total "by group" page. Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0350	mITT	AE18	Summary of All Serious Treatment Emergent Adverse Events by Maximum Grade and Treatment Arm	Treatment emergent only. Use combined PTs with footnote "Preferred terms are combined."	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Use “Adverse Event” (rather than “Preferred Term”) as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	
3.0360	mITT	OAE07	Summary of All Study-Treatment Related Serious Adverse Events by Maximum Grade	Treatment emergent only. Add total "by group" page. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0370	mITT	OAE07	Summary of All T-cell Infusion Serious Adverse Events by Maximum Grade	Treatment emergent only. Add total "by group" page. Use combined PTs with footnote “Preferred terms are combined.” Use “Adverse Event” (rather than “Preferred Term”) as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	SAC
3.0380	mITT	OAE07	Summary of All Lymphodepletion-Related Serious Adverse Events by Maximum Grade	Treatment emergent only. Add total "by group" page. Use combined PTs with footnote “Preferred terms are combined.”	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Use "Adverse Event" (rather than "Preferred Term") as header. Present grades 3+4+5 combined (as in OAE01) rather than 3+4. Align w/study 208469 (MRCLS).	
3.0390	ITT	AE3	Summary of Fatal Adverse Events by Preferred Term	Add Total column. Do not produce if <5 subjects have fatal AE. Do not use combined PTs. Align w/study 208469 (MRCLS).	SAC
3.0400	mITT	AE3	Summary of Study-Treatment Related Fatal Adverse Events	Treatment emergent only. Add Total column. Use combined PTs with footnote "Preferred terms are combined." Use "Adverse Event" (rather than "Preferred Term") as header. Align w/study 208469 (MRCLS).	SAC
3.0410	ITT	AE3	Summary of All Serious Study-Treatment Related AEs by Overall Frequency	Add Total column. Do not use combined PTs. Align w/study 208469 (MRCLS).	SAC
Deaths					
3.0420	mITT	DD1	Summary of Deaths	IDSL Add Total column. Report time from T-cell infusion to death with median, min, max, 1st Q, 3rd Q in months, >30 days or <=30 days. Only report Alive at Last Contact (do not report follow up ongoing/ended).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Report primary cause of death categories corresponding to those captured on MM Combo eCRF. Align w/study 208469 (MRCLS).	
Laboratory: Chemistry					
3.0430	mITT	LB1	Summary of Chemistry Changes from Baseline	ICH E3. Add total panel. Align w/study 208469 (MRCLS).	SAC
3.0440	mITT	OLB9C	Summary of Worst-Case Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline	ICH E3 Include total panel. Report Week 4 and Week 15 visits plus Worst-case post-baseline only. For labs that are gradable by CTCAE v4.03. Align w/study 208469 (MRCLS).	SAC
3.0450	mITT	OLB11C	Summary of Worst-Case Chemistry Results Relative to Normal Range Post-Baseline Relative to Baseline	ICH E3 Include total panel. Do not report by visit. For labs that are NOT gradable by CTCAE v4.03. Add footnote “Only tests that are not gradable by CTCAE are summarized.” Align w/study 208469 (MRCLS).	SAC
Laboratory: Hematology					
3.0460	mITT	LB1	Summary of Hematology Changes from Baseline	ICH E3. Add total panel. Align w/study 208469 (MRCLS).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.0470	mITT	OLB9C	Summary of Worst-Case Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline	ICH E3 Include total panel. Report Week 4 and Week 15 visits plus Worst-case post-baseline only. For labs that are gradable by CTCAE v4.03. Align w/study 208469 (MRCLS).	SAC
3.0480	mITT	OLB11C	Summary of Worst-Case Hematology Results Relative to Normal Range Post-Baseline Relative to Baseline	ICH E3 Include total panel. Report Week 4 and Week 15 visits plus Worst-case post-baseline only. For labs that are NOT gradable by CTCAE v4.03. Add footnote “Only tests that are not gradable by CTCAE are summarized.” Align w/study 208469 (MRCLS).	SAC
Laboratory: Other Tests					
3.0490	mITT	LB1	Summary of Other Laboratory Changes from Baseline	ICH E3 Add total panel. Include all "other" (non-chemistry, non-hematology) quantitative lab tests (i.e., coagulation, immunology, endocrine, urinalysis, and biomarker). Align w/study 208469 (MRCLS).	SAC
3.0500	mITT	OBL9C	Summary of Worst-Case Other Laboratory Results by Maximum Grade Increase Post-Baseline Relative to Baseline	ICH E3 Include total panel. Report Week 4 and Week 15 visits plus Worst-case post-baseline only. For labs that are gradable by CTCAE v4.03.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				Include all "other" (non-chemistry, non-hematology) quantitative lab tests (i.e., coagulation, immunology, endocrine, urinalysis, and biomarker). Align w/study 208469 (MRCLS).	
3.0510	mITT	OLB11C	Summary of Worst-Case Other Laboratory Results Relative to Normal Range Post-Baseline Relative to Baseline	ICH E3 Include total panel. Do not report by visit. For labs that are NOT gradable by CTCAE v4.03. Add footnote “Only tests that are not gradable by CTCAE are summarized.” Include all "other" (non-chemistry, non-hematology) quantitative lab tests (i.e., coagulation, immunology, endocrine, urinalysis, and biomarker). Align w/study 208469 (MRCLS).	SAC
Performance Status					
3.0520	mITT	PS1A	Summary of ECOG Performance Status	ICH E3 Add Total column. Only summarize baseline and last assessment. Align w/study 208469 (MRCLS).	SAC
3.0530	mITT	PS3A	Summary of Change in ECOG Performance Status from Baseline	ICH E3 Add Total column. Include best and worst case. Align w/study 208469 (MRCLS).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
ECG					
3.0540	mITT	EG1	Summary of ECG Findings	IDSL Add Total column. "Clinically significant change from baseline" in this standard shell is not collected in this study so cannot be reported; drop from the display. Align w/study 208469 (MRCLS).	SAC
3.0550	mITT	OECG1C	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category	IDSL Include total panel. Do not report by visit. QTcB and QTcF should be reported in this same table but summarized separately. QTcB and QTcF values should not be derived. Align w/study 208469 (MRCLS).	SAC
3.0560	mITT	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL Include total panel. QTcB and QTcF should be reported in this same table but summarized separately. Align w/study 208469 (MRCLS).	SAC
3.0570	mITT	OECG2C	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category	IDSL Include total panel. Do not report by visit.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
				QTcB and QTcF should be reported in this same table but summarized separately. Align w/study 208469 (MRCLS).	
Vital Signs					
3.0580	mITT	VS1	Summary of Change from Baseline in Vital Signs	ICH E3 Include total panel. Include weight, temp, DBP, SBP pulse rate, respiratory rate. Align w/study 208469 (MRCLS).	SAC
3.0590	mITT	OVT1C	Summary of Worst-Case Heart Rate Results Relative to Normal Range Post-Baseline Relative to Baseline	IDSL Include total panel. Do not summarize by visit. Align w/study 208469 (MRCLS).	SAC
3.0600	mITT	OVT2C	Summary of Worst-Case Blood Pressure Results by Maximum Grade Increase Post-Baseline Relative to Baseline	IDSL Include total panel. Do not summarize by visit. Align w/study 208469 (MRCLS).	SAC
Replication Competent Lentivirus (RCL)					
3.0610	mITT	[Non-Standard] SAFE_T3	Summary of Replication Competent Lentivirus Positive	Please produce even if positive counts are low or zero. Align w/study 208469 (MRCLS).	SAC
3.0620	mITT	[Non-Standard] SAFE_T3	Summary of Subjects Showing >1% Gene Marked PBMCs 1 Year Post-Treatment	Define 1 year conservatively as at least 360 days since infusion or month 12 visit. Align w/study 208469 (MRCLS).	SAC

14.12.8. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Duration Plots					
3.0630	mITT	[Non-Standard] SAFE_F2	Plot of Duration on Treatment Phase	(1) Show all subjects on the same plot; do not show by treatment arm. Instead, add Arm label as an additional column to the right of Age/Sex. (2) Sort the Subject ID (y-axis) in ascending order of Arm, Best Overall Response, and Duration on Study. (3) Use x-axis label of "Time Since T-cell Infusion (months)" and begin the axis (origin) at the start of lymphodepletion. (4) Remove all indication of diagnosis and prior therapies. (5) Show symbols or colored lines for: first confirmed response (star), SAE (asterisk), progression (diamond or other polygon), transfer to LTFU study (dot), ongoing participation in the study (blue line), date of first pembro (triangle), and ongoing status (at the time of analysis, arrow pointing to the right). (6) Show first date of progression, even if not confirmed. Please add a footnote to explain which subjects did not have confirmed progression. Not aligned w/study 208469 (MRCLS).	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.0640	mITT	[Non-Standard] SAFE_F1	Plot of Prior Therapy Information by Treatment Arm	(1) Show all subjects on the same plot; do not show by treatment arm. Instead, add Arm label as an additional column to the right of Age/Sex. (2) Sort the Subject ID (y-axis) in ascending order of Arm, Best Overall Response, and Duration on Study. (3) Use x-axis label of "Time Since T-cell Infusion (months)". Begin the axis (origin) at the earliest diagnosis date (i.e., make sure the axis is expansive enough to show all diagnosis dates). End the axis at point of T-cell infusion. (4) Show symbols or colored lines for: Diagnosis, SAE, Leukapheresis, Surgery, Radiotherapy, Stem Cell Therapy (note that stem cell therapy + conditioning chemo represent a single regimen), Systemic Therapy Regimen 1, Regimen 2, Regimen 3, etc., and Lymphodepleting Chemotherapy. (5) Consider imputation of prior therapy dates in order to show duration on therapy. Add footnote: "Note: Start and end dates of prior therapy are imputed for missing day.' Not aligned w/study 208469 (MRCLS).	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory					
3.0650	mITT	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin – eDISH	IDSL Include both treatment arms on same plot (same axes), with arms differentiated by color or pattern. Align w/study 208469 (MRCLS).	SAC
3.0660	mITT	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT	IDSL Include both treatment arms on same plot (same axes), with arms differentiated by color or pattern. Align w/study 208469 (MRCLS).	SAC
3.0670	mITT	[Non-Standard] SAFE_F3	Plot of Hematology Data Over Time	Produce a separate plot for neutrophils, lymphocytes, platelets, and hemoglobin (page-by lab test) Legend should list subjects by treatment arm, but subjects should not be grouped by treatment arm in the figure (each subject should have a unique color) X-axis units should be days starting at day -14.and ending at day 90. Not aligned w/study 208469 (MRCLS)	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
ECG					
3.0680	mITT	OECG4	QTc Shifts from Baseline to Worst-Case Post Baseline	IDSL Include both treatment arms in same plot (same axes), with arms differentiated by color or pattern. Create separate plots for the 2 QTc correction methods (QTcB vs. QTcF). Align w/study 208469 (MRCLS).	SAC

14.12.9. Biomarkers Tables

Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Anti-NY-ESO-1 Antibodies					
3.0690	mITT	[Non-Standard] BIO_T1	Summary of Anti-NY-ESO-1 TCR(c259) Antibodies (ATA)	Align w/study 208469 (MRCLS). Only if data are available	SAC

14.12.10. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Persistence of NY-ESO-1^{c259}T					
4.0010	mITT	[Non-Standard] PK_T1	Summary of Derived Persistence Parameters	Only report peak expansion (i.e. not by scheduled visits). Report overall and by responders vs. non-responders. Add total "by group" page. Display by type of persistence if BMMC data is available. Add footnote: "Note: Samples collected within 4 days of day 28 are treated as day 28 when calculating AUC(0-28)" Not aligned w/study 208469 (MRCLS).	SAC
4.0020	mITT	[Non-Standard] PK_T2	Summary of Log-Transformed Derived Persistence Parameters	Report overall and by responders vs. non-responders. Add total "by group" page. Display by type of persistence if BMMC data is available. Add footnote: "Note: Samples collected within 4 days of day 28 are treated as day 28 when calculating AUC(0-28)" Not aligned w/study 208469 (MRCLS).	SAC

14.12.11. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Persistence of NY-ESO-1^{c259}T					
4.0030	mITT	[Non-Standard] PK_F2	Distribution of Peak Expansion	Updated to dot plot. Please show both treatment arms on the same plot, with different colors for each arm. Plot by responders vs. non-responders. Page by type of persistence if BMMC data is available. Not aligned w/study 208469 (MRCLS).	SAC
4.0040	mITT	[Non-Standard] PK_F1	Persistence Profile by Subject	Plot by treatment arm. Present with x-axis sufficient to see all follow-up. Add subject numbers into the legend, add symbols at analysis timepoints, and differentiate subjects with symbols and tine types X-axis and Y-axis should be same for each treatment arm. Label X-axis “Study Day” rather than “Time from T-cell Infusion (Days)”. Not aligned w/study 208469 (MRCLS).	SAC
4.0050	mITT	[Non-Standard] PK_F1	BMMC Persistence Profile by Subject	Present with x-axis sufficient to see all follow-up. Not aligned w/study 208469 (MRCLS).	SAC

14.12.12. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
0010	Screened	ES7	Listing of Reasons for Screen Failure	Only include subjects that were screen failures; do not include "Run-In" elements or optional column "Type of Failure" Note that rescreened subjects that screen fail twice will appear twice in listing. Report as captured on CRF	SAC
0020	ITT	ES2	Listing of Reasons for Study Withdrawal	ICH E3 Do not include columns "Reason Term(s)", "Was a follow-up phone contact attempted 3 times?" & " Was a follow-up certified letter mailed?" from GSK standard mock as not collected in this study. Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
0030	ITT	[Non-Standard] POP_L5	Listing of Study Treatment Status	ICH E3 Present this listing by treatment arm. Please include: Leukapheresis date, Lymphodepletion, T Cell Infusion Date, Time between Leukapheresis and T Cell Infusion, Transduced Dose, Completed Treatment Phase, Date of Discontinuation/Completion of Treatment Phase/Duration on Study (days), Reason for Discontinuation/Completion of Treatment Phase, End of Study Status Reason, and Death Date. Please insert a footnote: "Duration on Study refers to duration of follow-up on treatment phase." Not aligned w/study 208469 (MRCLS).	SAC
0040	mITT	ODMOD12A	Listing of Dose Delays (Pembrolizumab)	Do not include 'Primary reason for Delay/Specify' column Insert footnote: "Note: Duration of Delays = actual start date of current dose – expected start date of dose. Expected start date of dose=actual start date of previous dose + 21." Not aligned w/study 208469 (MRCLS)	SAC
0050	mITT	SD2	Listing of Reasons for Study Treatment Discontinuation (Pembrolizumab)	ICH E3 Arm 2 only Not aligned w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Populations Analysed					
0060	Screened	SP3	Listing of Subjects Excluded from Any Population	ICH E3 Include all subjects in population for display. Include columns to indicate exclusion ('Y') from Enrolled, ITT, and mITT populations. Drop "Date of Deviation/ Study day" and "Category/Coded Term" columns. Populate "Criteria" column with reason for exclusion from first: "SUBJECT NOT ELIGIBLE FOR APHERESIS", "SUBJECT NOT APHERESED", "SUBJECT NOT INFUSED". Align w/study 208469 (MRCLS).	SAC
Protocol Deviations					
0070	ITT	DV2	Listing of Important Protocol Deviations	ICH E3 Align w/study 208469 (MRCLS).	SAC
0080	ITT	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3 Align w/study 208469 (MRCLS).	SAC
Demographic and Baseline Characteristics					
0090	ITT	DM2	Listing of Demographic Characteristics	ICH E3 Present this listing by treatment arm. Add BMI, BSA, and Race. Align w/study 208469 (MRCLS).	SAC
Prior and Concomitant Medications					
0100	ITT	BP4	Listing of Blood Products	Include all blood products. Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
0110	ITT	CM3	Listing of Medications	IDSL Include all collected medications, do not subset on concomitant medication study phase Replace "Started Pre-Trial" column with "Prior / Concomitant" (identified per Appendix 4)	SAC
Exposure					
0120	ITT	[Non-Standard] POP_L3	Listing of Leukapheresis, Lymphodepletion, T-cell, and Pembrolizumab Infusion Dates	ICH E3 With the exception of Pembro being added, this listing should align w/study 208469 (MRCLS).	SAC
0130	ITT	[Non-Standard] POP_L1	Listing of Exposure to Lymphodepletion Chemotherapy	ICH E3 One column for Fludarabine dose Align w/study 208469 (MRCLS). As per MRCLS, please remove MESNA.	SAC
0140	ITT	[Non-Standard] POP_L2	Listing of Exposure to T-cell Infusion	ICH E3 Align w/study 208469 (MRCLS).	SAC
0150	ITT	OEX8B	Listing of Exposure to Pembrolizumab	ICH E3 For subjects in Arm 2 only. Replace Cycle with Visit. Not aligned w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events					
0160	ITT	AE8	Listing of All Adverse Events	ICH E3 Present this listing by treatment arm. Report time from first T-cell Infusion. Use “Time Since T-cell Infusion” instead of Time Since First Dose/Time Since Last Dose. Add MM Combo specific "action taken" column. With the exception of the added “action taken” (specific to MM Combo), this listing should align w/study 208469 (MRCLS).	SAC
0170	ITT	AE8	Listing of Adverse Events Leading to Dose Interruption, Dose Reduction, or Permanent Discontinuation of Pembrolizumab	For subjects in Arm 2 only. Not aligned w/study 208469 (MRCLS).	SAC
0180	ITT	[Non-Standard] SAFE_L1	Listing of Delayed Adverse Events	ICH E3 Report time from first T-cell Infusion. Use “Time Since T-cell Infusion” instead of Time Since First Dose/Time Since Last Dose.	SAC
0190	ITT	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3 All AEs. Align w/study 208469 (MRCLS).	SAC
0200	ITT	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events of Special Interest					
0210	mITT	[Non-Standard] SAFE_L1	Listing of AESI (Focused List)	Use Focused Scope List. Sort by USUBJID, AEDECOD, ASTDT, AENDT. Present by treatment arm and by AESI. Align w/study 208469 (MRCLS).	SAC
0220	mITT	[Non-Standard] SAFE_L1	Listing of Haematopoietic Cytopenias (Comprehensive List)	Use Comprehensive Scope List. Sort by USUBJID, AEDECOD, ASTDT, AENDT. Present by treatment arm. Align w/study 208469 (MRCLS).	SAC
0225	mITT	[Non-Standard] SAFE_L6	Listing of CARTOX and ICE Score	Align w/study 208469 (MRCLS)	SAC
Serious and Other Significant Adverse Events					
0230	ITT	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3 Align w/study 208469 (MRCLS).	SAC
0240	ITT	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3 Add PAN12. Align w/study 208469 (MRCLS).	SAC
0250	ITT	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events	If data exists	SAC
Death					
0260	ITT	DD3	Death Profile	Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Hepatobiliary (Liver)					
0270	ITT	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	IDSL Update columns "Time Since First / Last Dose (days)" of LIVER5 mock with "Time Since First T-cell Infusion" & "Time Since Last T-cell Infusion". Align w/study 208469 (MRCLS).	SAC
0280	ITT	LIVER15	Liver Stopping Event Profile	IDSL Update variables "Time Since First / Last Dose (days)" of LIVER15 mock with "Time Since First T-cell Infusion" & "Time Since Last T-cell Infusion". Align w/study 208469 (MRCLS).	SAC
0290	ITT	LIVER13	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline	IDSL Please make sure this is derived correctly by considering all liver function criteria specified in the LIVER IDSL doc. Align w/study 208469 (MRCLS).	SAC
All Laboratory					
0300	ITT	LB5A	Listing of All Laboratory Data	ICH E3 Combining all laboratory data (chem, hem, etc.) in one listing, including biomarker data but NOT including urinalysis data. Align w/study 208469 (MRCLS).	SAC
0310	ITT	UR2A	Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance	ICH E3 Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Replication Competent Lentivirus (RCL)					
0320	mITT	LB5A	Listing of VSV-G DNA (RCL) Data	Align w/study 208469 (MRCLS).	SAC
0330	mITT	[Non-Standard] SAFE_L2	Listing of Integration Site Analysis Results	This is a supplemental display to the table summary "Summary of Subjects Showing Monoclonality of Genetically Modified T-cell Population" (which uses SAFE_T3). Create only if data are available. Align w/study 208469 (MRCLS).	SAC
Pharmacokinetic					
0340	mITT	[Non-Standard] PK_L1	Listing of Persistence Data	Present this listing by treatment arm. Present by persistence type if BMMC data are available. Show time to loss of 25%, 50% and 75% of peak expansion, peak expansion, time to peak expansion, and AUC(0-28). With the exception of the added AUC(0-28) parameter, this listing should align w/study 208469 (MRCLS).	SAC
Biomarkers					
0350	mITT	[Non-Standard] BIO_L1	Listing of Anti-NY-ESO-1 Antibodies	Align w/study 208469 (MRCLS). Only if data are available	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
ECG					
0360	ITT	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL Update PCI footnote to use oncology definition "…Clinical Importance is defined as Grade 2 or Higher (QTc>480), or QTc increase of >30 msec…" (as in OECG5A). Align w/study 208469 (MRCLS).	SAC
0370	ITT	EG5	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL "Clinically significant change from baseline" and "Clinically Significant Abnormality" in this standard shell are not collected in this study so cannot be reported – drop from display. Align w/study 208469 (MRCLS).	SAC
Vital Signs					
0380	ITT	OVT7A	Listing of Vital Signs with Values of Potential Clinical Importance	IDSL Align w/study 208469 (MRCLS).	SAC
Response					
0390	ITT	[Non-Standard] EFF_L2	Listing of Investigator-Assessed Responses (with confirmation) (IMWG 2016)	Present this listing by treatment arm. Please ensure that an additional column is included to display "by-visit" Confirmed Response, to the right of the column of "by-visit" responses. Not aligned w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Time to Event					
0400	mITT	TTE9	Listing of Investigator-Assessed Time to Response (IMWG 2016)	Use T-cell infusion date. Include optional "New Anti-Cancer Therapy Start Date" column. Align w/study 208469 (MRCLS).	SAC
0410	mITT	TTE9	Listing of Investigator-Assessed Duration of Response (IMWG 2016)	Present this listing by treatment arm. Add Initial Confirmed Response. Use T-cell infusion date. Include optional "New Anti-Cancer Therapy Start Date" column. Include footnote: "Note: Duration of Response is defined as the interval between the initial date of the confirmed response (sCR, CR, VGPR, or PR) and the date of confirmed progressive disease or death among subjects with a confirmed response per IMWG 2016." Align w/study 208469 (MRCLS).	SAC
0420	mITT	TTE9	Listing of Investigator-Assessed Progression Free Survival (IMWG 2016)	Present this listing by treatment arm. Use T-cell infusion date Include optional "New Anti-Cancer Therapy Start Date" column. Similar to the footnote used in the DoR listing above, add a footnote that defines PFS as including confirmed progressive disease. Align w/study 208469 (MRCLS).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
0430	mITT	TTE9	Listing of Overall Survival	Use T-cell infusion date. Exclude optional "New Anti-Cancer Therapy Start Date" column. Align w/study 208469 (MRCLS).	SAC

14.12.13. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Disease Characteristics					
0440	ITT	DC3	Listing of Disease Characteristics at Initial Diagnosis	Present this listing by treatment arm. Please report: date of initial diagnosis, time from initial diagnosis to screening ICF signed (in months), stage at diagnosis, histologic type, % clonal bone marrow plasma cells, presence and type of end organ damage, presence and type of plasmacytoma, and chromosomal aberrations. Remove primary neoplasm type under study and study specific category (as they are not relevant) and remove histologic grade (as it is not collected). Not aligned w/study 208469 (MRCLS).	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
0450	ITT	[Non-Standard] POP_L4	Listing of Disease Characteristics at Screening	Present this listing by treatment arm. Please report: type of multiple myeloma, HLA status (date, allele 1, allele 2), NY-ESO-1 biopsy date and status, LAGE-1a (date, status), number of systemic therapy / radiotherapy regimens prior to leukapheresis, and receipt of stem cell transplant/therapy prior to leukapheresis (Y/N) for each of 2 subtypes (autologous vs. allogeneic). Also, use the new derivation of lines of systemic therapy (i.e., count systemic therapy + conditioning chemo associated w/stem cell therapy) – please add a footnote that makes this clear. Not aligned w/study 208469 (MRCLS).	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Anti-Cancer Therapies					
0460	ITT	AC6	Listing of Prior Systemic Anti-Cancer Therapy	Present this listing by treatment arm. In addition to the Most Recent Response, please include “Best Response” in the same column (to be shown first) and “MRD” (to be shown last). Remove “Reason for Stopping” (as not collected for prior systemic therapy) and replace it with “Disease Refractory to Regimen (Y/N)”. Add "Intent" (i.e., treatment intent). Add final column with header of "Started after Leukapheresis?/Bridging Therapy?" “Note: This listing includes all systemic therapy prior to lymphodepletion.” Sort by regimen. Conditioning chemotherapies (associated with stem cell therapy) and stem cell therapy should appear in this listing Not aligned w/study 208469 (MRCLS).	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
0470	ITT	AC7	Listing of Anti-Cancer Radiotherapy	List all radiotherapy before lymphodepletion and flag the ones occurring between leukapheresis and lymphodepletion as "Started after Leukapheresis". Use T-cell infusion date. Include optional “New Anti-Cancer Therapy Start Date” column. Add final column with header of "Transition Therapy" Add footnotes: “Note: This listing includes all radiotherapy received by the subject.” “Note: Transition therapies include all therapy received after leukapheresis and before lymphodepletion.” Align w/study 208469 (MRCLS).	SAC
0480	ITT	FAC3	Listing of On-Study Anti-Cancer Therapy	Include “Time to Progression (Days)” but not “Overall Survival (Days)”. Use date of "first progression" even if not confirmed for TTP column. Footnote any subject with unconfirmed PD. Includes radiotherapy, systemic therapy, and stem cell therapy Align w/ study 208469 (MRCLS)	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Symptoms, Concomitant Medications and Procedures Related to Adverse Events of Special Interest					
0490	ITT	[Non-Standard] SAFE_L4	Listing of Symptoms, Concomitant Medications, and Procedures Related to Cytokine Release Syndrome (CRS)	Present this listing by treatment arm. Add column showing list of all symptoms. Align w/study 208469 (MRCLS).	SAC
0500	ITT	[Non-Standard] SAFE_L5	Listing of Symptoms, Concomitant Medications, and Procedures Related to Graft versus Host Disease (GvHD)	Present this listing by treatment arm. Add column showing list of all symptoms. Align w/study 208469 (MRCLS).	SAC
Surgical Procedures					
0510	ITT	OSP3	Listing of Prior Cancer-Related Surgical Procedures	List all surgeries before lymphodepletion and flag the ones occurring between leukapheresis and lymphodepletion as "Started after Leukapheresis?" List Surgery Intent and Site and Date of Surgery. Add footnote: “Note: This listing includes all cancer-related surgeries prior to T-cell infusion.” Align w/study 208469 (MRCLS).	SAC
0520	ITT	OSP3	Listing of On-Study Cancer-Related Surgical Procedures	List Site and Date of Surgery. Align w/study 208469 (MRCLS).	SAC

14.13. Appendix 13: Example Mock Shells for Data Displays

Data Display Specification will be made available on request

14.14. Appendix 14: Combined Preferred Terms

Combined Term	MedDRA Preferred term	PT Code	
Anemia/RBC decreased	Anemia	10002034	PT
Cytokine Release Syndrome (CRS)	Cytokine Release Syndrome	10052015	PT
	Cytokine Storm	10050685	PT
Acute GVHD - Skin	Acute graft versus host disease in skin	10066262	PT
Acute GVHD - Gut (Liver and Intestine)	Acute graft versus host disease in liver	10066263	PT
	Acute graft versus host disease in intestine	10066264	PT
Acute GVHD - Other (Lung, Bone Marrow, not specified)	Acute graft versus host disease	10066260	PT
Chronic GVHD - Skin	Chronic graft versus host disease in skin	10072159	PT
Chronic GVHD - Gut (Liver and Intestine)	Chronic graft versus host disease in liver	10072160	PT
	Chronic graft versus host disease in intestine	10072158	PT
Chronic GVHD Other - (Lung, Bone Marrow, not specified)	Chronic graft versus host disease	10066261	PT
Unspecified GVHD - Skin	Graft versus host disease in skin	10064675	PT
Unspecified GVHD - Gut (Liver and Intestine)	Graft versus host disease in liver	10064676	PT
	Graft versus host disease in gastrointestinal tract	10075160	PT
Unspecified GVHD - Other (Lung, Bone Marrow, not specified)	Graft versus host disease	10018651	PT
	Graft versus host disease in eye	10074563	PT
	Graft versus host disease in lung	10067742	PT
	Prophylaxis against graft versus host disease	10053239	PT

Combined Term	MedDRA Preferred term	PT Code	
	Transfusion associated graft versus host disease	10070895	PT
	Engraftment syndrome	10050684	PT
Leukopenia/WBC decreased	White blood cell count decreased	10047942	PT
	Leukopenia	10024384	PT
Lymphopenia/Lymphocyte count decreased	Lymphocyte count decreased	10025256	PT
	CD4 lymphocytes decreased	10007839	PT
	CD8 lymphocytes decreased	10056283	PT
Neutropenia/Neutrophil count decreased	Neutrophil count decreased	10029366	PT
	Neutropenia	10029354	PT
Rash/Rash maculo-papular	Rash maculo-papular	10037868	PT
	Rash	10037844	PT
	Rash erythematous	10037855	PT
Thrombocytopenia/Platelet count decreased	Platelet count decreased	10035528	PT
	Thrombocytopenia	10043554	PT
	MedDRA version 21.1 for PT codes		

14.15. Appendix 15: Adverse Event Collapsing Rules

1. Collapsing AE Segments with a Common AE Preferred Term (PT) into Unique Events based on the Start and End Dates

For each unique subject, the AE records (segments) with the same AE preferred term will be collapsed into one unique AE event based on the start and end dates below.

1.1. Multiple AE Segments with Overlapped or Continuous Start/End Dates

Multiple AE segments with a common preferred term (PT, variable=ADAE.AEDECOD) that occurred around the same time; defined as:

If a segment starts no more than one day (i.e., ≤ 1 day) prior, on, or after the previous segment's end date, it is considered as an 'event'.

If the gap between the start date of a segment and the end date of previous segment is greater than one complete day (i.e., > 1 day), then consider these segments as different events.

If partial start or end dates for any AE segments, then consider these segments as separate events.

*** **NOTE: Handling of partial dates or completely missing dates**

Partial dates or completely missing dates will not be imputed.

The reason for not using imputed dates is due to the small number of partial / or completely missing dates. Furthermore, using imputed dates might create additional error of up to 30 days off for the AE start or AE end dates, and can be up to 60 days off for the duration of AE.

1.2.Sort Adverse Events (AE)

For any AE event identified above:

Sort the AEs segments by study ID (ADAE.STUDYID), unique subject ID (ADAE.USUBJID), AE preferred term (ADAE.AEDECOD), AE start date (ADAE.AESTDTC), and AE end date (ADAE.AEENDTC). The sorting will include all AE segments with complete or partial start / end dates.

1.3.Create Derived Variables in ADAE ADaM SAS Dataset

Based on the ADAE dataset sorted above under Section 1.2, for each unique subject, create the following derived variables in the ADAE ADaM SAS dataset:

1) **ANL01FL: Flag for the unique AE**
   a) **Collapsed AE Segments**

      For collapsed AE segments. based on the ADAE dataset sorted above under Section 1.2:

      - derive the flag variable: **ANL01FL=”Y” on the first record for each collapsed AE (i.e. the earliest segment within each collapsed AE with the same ADAE.AEDECOD)** . In case if the AE segment of the collapsed AEs started before Lymphodepletion and ending after it, then populate the ANL01FL=’Y’ on very first Treatment emergent record. If there is only one record (segment) which started before lymphodepletion and ended after lymphodepletion then populate ANL01FL=’Y’ on that record only.
      - **Otherwise ANL01FL="" (Missing).**

   b) **AE Events Comprised of a Single Row (No Collapsing Needed)**
      - derive the flag variable: **ANL01FL=”Y” for each single segment AE event**.

2) EVTSEQ: Sequence number of each unique AE with the same PT

Create a sequence number, EVTSEQ, for each unique AE within the same ADAE.AEDECOD.

For each unique subject within each unique AE preferred term, this variable will be recorded as **the sequential number to identify all unique adverse events (including both single segment events (i.e., no collapsing needed) and collapsed events from multiple segments) based on the sorting order chronologically addressed above under Section 1.2.**

a) **Collapsed AE Segments**

Each collapsed AE and its corresponding composed segments will have the same sequence numbers (i.e., if multiple segments/records are qualified for being collapsed into one unique AE (i.e., all those records will have same value for the derived variable EVTSEQ for that corresponding subject within the same collapsed AE).

b) **Single Segment AE Records**

Each single segment AE event (i.e., un-collapsed event) will have different unique sequence number separately

c) AE Segments with partial start or end dates

Each AE segment with partial start or end dates will have different unique sequence number starting from 99XXX, where XXX=001, 002, ...

*** NOTE:**

For those subjects who received 2 T-cell infusions, the sequential number will be based on both infusion periods combined (i.e., the assigned sequential number will be independent of T-cell infusion periods).