Division	:	Worldwide Development
Information Type	:	Statistical Analysis Plan (SAP)

TITLE PAGE

Protocol Title: A Phase I Study to Evaluate the Pharmacokinetics and Safety of Belantamab Mafodotin Monotherapy in Participants with Relapsed or Refractory Multiple Myeloma Who Have Normal and Varying Degrees of Impaired Renal Function (DREAMM 12)

Protocol Number: 209626

Compound Number: GSK2857916

Short Title: A Phase I Study of Belantamab Mafodotin in Multiple Myeloma Participants with Normal and Impaired Renal Function

Acronym: DREAMM12

Sponsor Name: GlaxoSmithKline Research & Development Limited

Regulatory Agency Identifier Number(s)

Registry	ID
Clintrials.gov	NCT04398745
IND	119333

TABLE OF CONTENTS

PAGE

VERSION HISTORY

This Statistical Analysis Plan (SAP) for study 209626 is based on the protocol dated 15-Jun-2022 (Version: GSK Document Number TMF-14740476).

Table 1 SAP Version History Summary

SAP Version	Effective Date	Protocol Version (Date) on which SAP is Based	Change	Rationale
1	14May2020	Original V1 (26-Feb-2020)	Not Applicable	Original version
2	06 Oct 2022	Amendment 3 (15-Jun-2022)	• Minor clarifications of typos and language throughout	• Updates to align with PA3
			• Change in layout of SAP	• Updates due to template change
			• PK Evaluable Set added and primary endpoint analysis will be based on the PK evaluable set, but listings will include all participants in the PK Analysis Set	• To ensure the primary analysis is based on robust data
			• Safety/PK analysis and interim analysis combined	• See justification in changes to protocol defined statistical analysis plan section

			• Clarified the groups to be compared in analyses • Change in groups for comparison of 'normal' renal function to 'normal/mildly impaired' throughout • eGFR sensitivity analyses included for several displays • included supportive analysis to evaluate iGFR and eGFR concordance	• Due to the protocol amendment relating to the use of iGFR instead of eGFR to define renal function. See justification in changes to protocol defined statistical analysis plan section.
			• Clarified displays to be included in the combined safety/pk and interim analysis	• Sufficient detail for outputs for inclusion not previously provided.
			• Baseline definition updated	• To clarify how re-screened participants will be handled • Remove ECG handling as this will not be summarized
			• Removed several PK parameters	• To align with intent of protocol and meet study specific requirements

			• Included a forest plot to compare the PK parameter ratio of geometric means	• To help visualize the data and ease of interpretation
			• Included treatment emergent definition • Clarified all AE summaries will be based on treatment-emergent definition but all AEs will be listed	• See justification in changes to protocol defined statistical analysis plan section
			• Additional AE displays included, including non-serious study treatment-related AEs, an alternative SAE table and liver displays	• Required for disclosure and other study reporting activities
			• Grade 5 AEs included in the AE Overview Summary, so that Grade 3+4+5 AEs are summarised	• To aide AE review
			• Clarifications for AESI displays including how to identify AESI and worst case hierarchy • Further details on AESI data to be summarized and	• To align with the approach across the project

			how this should be derived • Additional ocular assessment displays included and details aligned with data collection	
			• COVID-19 displays added	• Due to the emergence of the global COVID-19 pandemic
			• Some safety summaries removed (e.g., cardiovascular deaths)	• Redundant output as this will be included in other displays or limited data collection that is better supported by listings
			• Box plots for Urine PK parameters may be produced	• To support the planned summary tables
			• Efficacy analysis methods updated to consider Kaplan-Meier method in some cases if data permits. • Response confirmation algorithm details added • Assignment for progression and censoring dates clarified • Sensitivity analysis for duration of	• To align with the approach across project • See justification in changes to protocol defined statistical analysis plan section

			response included using alternative definition (considering death due to any cause)	
			• Pharmacodynamic and Biomarker Analyses included	• To provide details of the protocol defined exploratory endpoint analyses
			• Further clarifications and details of the study population analyses (including ocular history and risk factors) and data derivation rules included	• For transparency of the planned analyses
			• Some programming details have been removed (e.g. handling of partial dates) and included in the OPS	• To streamline SAP and align with internal processes
			• Reference to randomization removed throughout and where appropriate, replaced with first dose of study treatment (or similar wording)	• Study is not randomized

1. INTRODUCTION

The purpose of this SAP is to describe the planned analyses to be included in the Clinical Study Report(s) for Study 209626. Details of all the planned analyses, are provided.

1.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are detailed in Table 2.

Table 2 Changes to Protocol Defined Analysis Plan

Protocol Defined Analysis	SAP Defined Analysis	Rationale for Changes
PK analysis set used for all PK analyses	• PK evaluable set included: All participants in the safety analysis set who have at least 80% non-missing expected plasma PK data during the Cycle 1 profile (i.e., all Cycle 1 timepoints and Cycle 2 Day 1 pre-dose) This will be used for the primary analysis of PK data	• To ensure the primary analysis is based on robust data
3 analysis timepoints as detailed in Protocol Section 9.4, Table 18: - Safety/PK analysis - Interim Analysis - Primary/Final Analysis	2 analysis timepoints as detailed in SAP Section 4.1.1, Table 3: - Combined safety/pk and Interim Analysis - Primary/Final Analysis	CCI [redacted]

Protocol Defined Analysis	SAP Defined Analysis	Rationale for Changes
Time to progression is defined as the time from **randomization** until the earliest date of PD or death due to PD per IMWG. Descriptive statistics will be provided for participants with PD or who die due to PD and descriptive statistics of time on follow-up will be provided for participants who do not have PD.	TTP is defined as the time from **start date of treatment** until the earliest date of PD or death due to PD per IMWG. If data permit, distribution of TTP will be summarized using the Kaplan-Meier method by renal function group. The median, 25th and 75th percentiles of TTP will be estimated and corresponding 95% confidence intervals will be estimated using the Brookmeyer-Crowley method (1982). Kaplan-Meier Plots by renal function group will be produced if data permit. Otherwise, descriptive statistics will be provided for participants with PD or death due to PD.	Definition of endpoint revised to use start date of treatment instead of randomization date. The study is not randomized and analysis is based on the safety set. Kaplan-Meier method is more appropriate in order to account for censoring and not provide bias estimates, accounting for participants who remain on treatment without PD or death due to PD.
Time to response is defined as the time between the **date of randomization** and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better)	TTR is defined as the time between the **start date of treatment** and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better).	Definition of endpoint revised to use start date of treatment instead of randomization date. The study is not randomized and analysis is based on the safety set.
Duration of Response analysis: Descriptive statistics (mean, standard deviation, median, range) will be provided for participants who achieve PR or better, by censoring status.	If data permit, distribution of DoR for both definitions will be summarized using the Kaplan-Meier method by renal function group. The median, 25th and 75th percentiles of DoR will be estimated and corresponding 95% confidence intervals will be estimated using the Brookmeyer-Crowley method (1982). Kaplan-Meier Plots by renal function group will be produced if data permit. In addition, descriptive statistics will be provided for the following: • Participants who achieve PR or better until earliest PD or death due to PD	Descriptive summary for censored participants is not possible. Instead, the Kaplan-Meier method to account for censored participants has been included.

Protocol Defined Analysis	SAP Defined Analysis	Rationale for Changes
Section 9.4 of protocol: All summaries and analyses will be produced by enrolment group (Groups 1-2 or Groups 1-4 as applicable).	All summaries and analyses will be performed by renal function group.	Due to change in inclusion criteria switch from eGFR to iGFR, some participants drop out of the expected groups. To ensure the groups compared align with protocol intent, renal function groups will be compared. Those enrolled prior to the switch will be recategorized based on iGFR. AN "Other Renal Function" group is included for those with moderately impaired renal function based on iGFR.
Adverse Events: All AEs, serious or non-serious, will be reported from the start of treatment up to 70 days after the last dose of study treatment, until the participant withdraws consent for study participation, or until the participant starts subsequent anticancer therapy, whichever occurs first.	'On treatment' for AEs is defined as from the start of treatment until 70 days after the last dose of study treatment, until the participant withdraws consent for study participation. Treatment Emergent for AEs is defined as time from first dose to last dose plus 70 days or start of new anti-cancer therapy, whichever comes first. All AE tables will include treatment emergent AEs only, all AE listings will present all adverse events and will highlight AEs not on-treatment or treatment emergent.	Although all AEs will be reported in listings, as per the protocol, it is clarified that treatment-emergent AEs will be included in summary tables. This is to align with other studies in the project and what is considered clinically relevant and appropriate to understand the safety in this patient population.

1.2. Objectives and Endpoints

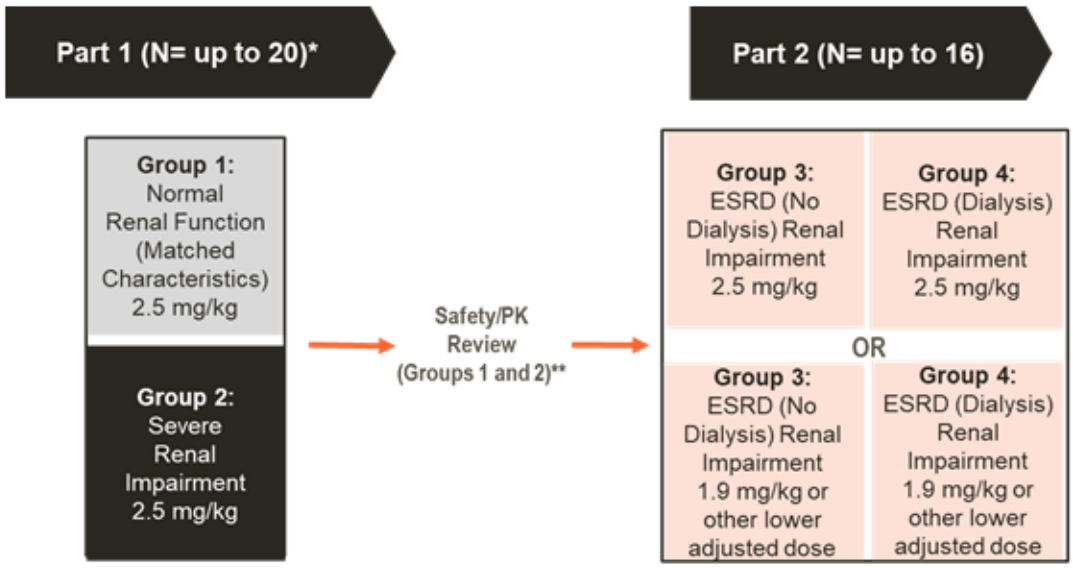
Objectives	Endpoints
Primary	**Primary**
• To describe the effects of renal impairment on the pharmacokinetics of belantamab mafodotin in participants with RRMM and with severe renal impairment, ESRD (not on dialysis) or ESRD (on dialysis) compared to participants with normal and mildly impaired renal function	• Plasma belantamab mafodotin, total mAb, and cys-mcMMAF pharmacokinetic parameters; as data permit
Secondary	**Secondary**
• To evaluate safety and tolerability using clinical parameters, including adverse events, vital signs, and clinical laboratory assessments in participants with RRMM who have normal or impaired renal functions	• Change from baseline in vital signs (blood pressure and heart rate), monitoring and incidence of adverse events, toxicity grading of clinical laboratory tests, and physical examinations
Exploratory	**Exploratory**
• To explore any relationship between PK and renal function parameters	• Relationship between belantamab mafodotin and cys-mcMMAF PK parameters (e.g., Cmax, AUC) and baseline renal function parameters (e.g., eGFR)
• To evaluate the recovery of cys-mcMMAF in urine in Part 1 only	• Urine recovery over 24 hours at several time points following the first dose
• To assess anti-drug antibodies (ADAs) against belantamab mafodotin	• Incidence and titers of ADAs against belantamab mafodotin
• To evaluate the clinical measures of efficacy of belantamab mafodotin in participants with RRMM who have normal or impaired renal function	• ORR (Overall Response Rate) • CBR (Clinical Benefit Rate) • DoR (Duration of Response) • TTR (Time to Response) • TTP (Time to Progression)

Objectives	Endpoints
• To explore the relationship between biological characteristics and clinical response	• Tumor and blood-based analyses of DNA, RNA and protein changes including but not limited to baseline and on-treatment sBCMA and BCMA expression on myeloma cells
• To evaluate the presence/concentrations of belantamab mafodotin and free cys-mcMMAF in tear fluid in participants with normal/mild or severely impaired renal function (Part 1 only) and explore relationship between tear fluid and plasma concentration	• Presence/concentrations of belantamab mafodotin and cys-mcMMAF in tear fluid at baseline and on treatment, as data permits • Relationship between tear fluid and plasma concentrations of belantamab mafodotin and of cys-mcMMAF, as data permits

Abbreviations: AUC = Area under the curve; BCMA = B-cell maturation antigen; Cmax = maximum observed concentration; DNA=deoxyribonucleic acid; ESRD = end stage renal disease; RNA= ribonucleic acid.

1.3. Study Design

Overview of Study Design and Key Features



*Participants in Group 1: N=8 (up to 12)
** Modifications to study eligibility criteria may be made during the study by amendment pending the result(s) of regular in-stream safety review(s) and/or as a result of the Safety/Pharmacokinetic (PK) review between the completion of the enrolment of Part 1 and the opening of enrolment in Part 2.
ESRD = end stage renal disease (eGFR <15 mL/min/1.73 m²) either not on hemodialysis or requiring hemodialysis

*Number of Participants in Group 1 enrolled can be 8 and up to 12, and 8 in Group 2.
** Modifications to study eligibility criteria may be made during the study by amendment pending the result(s) of regular
in-stream safety review(s) and/or as a result of the Safety/Pharmacokinetic (PK) review between the completion of the
enrolment of Part 1 and the opening of enrolment in Part 2. Dose may be adjusted for Part 2 to higher or lower than 1.9
mg/kg, or other adjusted dose.
ESRD = end stage renal disease (iGFR <15 mL/min) either not on hemodialysis or requiring hemodialysis

Design Features	• This is a Phase I, open-label study to assess the PK, safety, and tolerability of belantamab mafodotin monotherapy. • 32 (up to 36) participants with RRMM who have had at least 3 lines of prior treatment and have either normal or impaired renal functions will be enrolled. • Enrolled participants will be assigned to 1 of the 4 predefined groups based on renal function classification. Renal impairment will be classified based on the Individual Glomerular Filtration Rate (iGFR) using the Modification of Diet in Renal Disease (MDRD) formula [Levey, 2006] based on body surface area calculation (based on actual body mass/weight) [Mosteller, 1987] and according to FDA-defined categories of normal/mildly

Overview of Study Design and Key Features	

	impaired renal function, severe, ESRD (not on dialysis), or ESRD (on dialysis) [FDA DHHS, 2020].
	• The study is comprised of 2 parts and will enroll participants into 4 groups according to their iGFR levels.
	  ○ Part 1 will enroll participants with normal or mildly impaired renal function (Group 1; n=8 (up to 12) with matched baseline weight and baseline albumin levels to participants with severe renal impairment (Group 2; n=8).
	  ○ Part 2 will enroll up to 16 participants with end stage renal disease (ESRD) in 2 groups, targeting up to 8 in each group; those who are not on hemodialysis (Group 3; n=8), and those who are on hemodialysis (Group 4; n=8).
	  ○ As shown in the diagram above, the study will proceed from Part 1 to Part 2 based on the results from all participants enrolled in Part 1, Cycle 1 (Groups 1 and 2).
	• The study (in both parts) will include a Screening Phase, a Treatment Phase, and a Follow-up Phase.
	  ○ All participants will undergo screening assessments within 28 days of the initial dosing to determine eligibility for enrollment into the study.
	  ○ Participants are estimated to be treated for up to 15-18 months.
	  ○ The Safety Follow-up Phase will be at least 70 days after the last dose of belantamab mafodotin.
	  ○ Overall study duration is expected to be up to 48 months.
	• If participants prematurely discontinue the study prior to the end of Cycle 1, additional participants may be enrolled at the Sponsor's discretion in consultation with the Investigators.

Study treatment	• All participants in Part 1 will start on a dose of 2.5 mg/kg of belantamab mafodotin monotherapy administered by IV over approximately 30 minutes, administered on a Q3W schedule. • The starting dose in Part 2 will be decided based on the safety and PK results reported at the interim analysis performed after all participants in Part 1 have completed one cycle of treatment. • After Cycle 1, participants may have their dose modified (delayed or reduced) for toxicities as recommended in Section 6.6.2 of the protocol.
Study treatment Assignment	• No randomization will be used in this study, participants are assigned to single-arm cohorts based on their renal function status alone.
Planned analyses	• Details of the planned analyses are provided in Section 9.4 of the protocol.

2. STATISTICAL HYPOTHESES / SUCCESS CRITERIA

No formal hypothesis will be tested in this study; however, an estimation approach will be taken to characterize the PK of belantamab mafodotin (including ADC and the total antibody) and cys-mcMMAF in participants with severe renal impairment, ESRD (not on dialysis), and ESRD (on dialysis), compared with matched participants with normal/ mildly impaired renal function.

2.1. Multiple Comparisons and Multiplicity

Not applicable.

3. ANALYSIS SETS

Analysis Set	Definition / Criteria	Analyses Evaluated
Screened	• All participants who sign the ICF to participate in the clinical trial. Participants in this population will be used for screen failure summary.	• Study Population
Enrolled	• All participants who sign the ICF, pass the screening, and enter the study. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study are excluded from the Enrolled analysis set as they did not enter the study.	• Study Disposition
Safety	• All enrolled participants receiving at least 1 dose of belantamab mafodotin.	• Safety • Efficacy
Pharmacokinetic (PK)	• All participants in the safety analysis set who had at least one post first dose PK assessment	• PK
Pharmacokinetic (PK) Evaluable	• All participants in the safety analysis set who have at least 80% non-missing expected plasma PK data during the Cycle 1 profile (i.e., all Cycle 1 timepoints and Cycle 2 Day 1 pre-dose)	• PK

4. STATISTICAL ANALYSES

4.1. General Considerations

4.1.1. General Methodology

All summaries and analyses will be performed by renal function group. If appropriate, the ESRD participants data may also be combined into an 'All ESRD' group. Group 1 (normal and mildly impaired renal function) will be considered the control group for all comparisons, however, as groups 3 and 4 will not be matched to group 1, results of any comparisons between normal/mildly impaired and ESRD participants will be interpreted with caution.

The renal function group for each participant will be calculated using individual GFR (iGFR). Since the inclusion criteria was updated from eGFR to iGFR calculations in protocol amendment 2, some participants were enrolled prior to the amendment who do not meet the iGFR criteria appropriate for the study part. Any participants falling outside of the defined categories using will be grouped into "other".

The safety/PK and interim analyses have now been combined (as defined in Section 1). Details of the timing, endpoints and data used are detailed in Table 3.

Table 3 Details of Analyses to Be Performed

Analysis	Timing	Endpoints included	Data to be used
Combined Safety/PK and Interim Analysis	Approximately 6 months after the last participant in Part 1 has received first dose (and when all participants have completed Cycle 1)	All primary (PK) and secondary (safety) endpoints, including exploratory efficacy endpoints and other relevant exploratory endpoints	All data available for Part 1 participants only
Primary/Final Analysis	6 months after the last participant in Part 2 has received first dose	All endpoints	All data available at the time of the data cut

[1] Completed or withdrawn from the study prior to the relevant timepoint.

Full details of the outputs to be generated at each analysis time point will be provided in the Output and Programming Specification (OPS). Details of the outputs to be included in the Combined Safety/PK and Interim Analysis are provided in Appendix 3.

The combined safety/pk and interim analysis will include PK data up to the date that all participants in Part 1 complete Cycle 1, as a minimum. All other endpoints will include

data up to the date of PK data availability, approximately 6 months after the last participant has received first dose (or the majority of participants have at least 6 months follow-up).

All available PK, safety, and tolerability data (including the renal function and drug related toxicities, if any) will be evaluated by the GlaxoSmithKline (GSK) study team (including members from clinical, clinical pharmacology modeling/simulation group, safety, and statistics) and the study investigators to decide on the most appropriate dose to use in Part 2. Review of data will include (but will not be limited to) an evaluation of:

- Adverse events (AEs)/ Serious adverse events (SAEs)/ Adverse events of special interest (AESIs) (e.g., thrombocytopenia, infusion-related reactions [IRRs], corneal events) with grade and frequency of occurrence
- Number and reason for dose reductions and/or dose delays
- Number and grade of (S)AEs occurring upon rechallenge
- Number and grade of AEs leading to withdrawal from study treatment
- Laboratory data and assessments including renal and liver function data, including changes in toxicity grading
- Changes from baseline in vital signs
- Changes in physical examination findings (weight only)
- Plasma belantamab mafodotin, total mAb, and cys-mcMMAF pharmacokinetic data

Where data is available, all primary (PK) and secondary (safety) endpoints will be summarized. Additionally, in order to assess the risk:benefit profile, exploratory efficacy endpoints (including ORR, CBR, DoR, TTR and TTP) will be summarized. Urine PK data will also be included, if data permits. Supporting summaries to characterize the patient population, exposure and safety will be included.

Upon review of the data, the study team may decide on the following options:

- Initiate Part 2 with the 2.5 mg/kg Q3W dose
- Initiate Part 2 with a reduced dose of 1.9 mg/kg Q3W dose or other adjusted dose
- Stop the study if the benefit/risk is considered unfavorable regardless of any intervention.

Decisions will be made on an assessment of the comparative safety and PK profiles between Group 1 and Group 2. Consideration will be given to whether any differences in safety profile are due to the increased severity of renal disease in Group 2. The decision for Part 2 will be made considering results not only on their own, but with consideration of the background of further increased severity of disease in subsequent participants in Part 2.

Unless otherwise specified, data will be summarized using descriptive statistics: n, mean, standard deviation, median, minimum and maximum. Confidence intervals will be at 95% unless otherwise specified. Log-transformed data will have geometric mean, standard deviation on the log scale and coefficient of variation provided. Categorical data will be summarized as the number and percentage of participants in each category.

Participants who prematurely withdrew from study before the end of cycle 1 in Part 1 may be replaced.

It is anticipated that patient accrual will be spread thinly across centers and summaries of data by center would unlikely be informative and will not, therefore, be provided.

4.1.2. Baseline Definition

For all endpoints the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

For laboratory data, baseline will be the latest non-missing pre-dose value from the central laboratory. If no central laboratory value is available, the latest non-missing pre-dose value from the local laboratory will be used. However, for subjects with re-screened information the latest result will be used, regardless of whether this result is from the central or local laboratory.

Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing.

4.2. Primary Endpoint Analyses

For the primary endpoint analysis, tables and figures will be based on the PK evaluable analysis set. Relevant listings may be produced on the PK analysis set as long as the PK evaluable analysis set is clearly identified.

4.2.1. Definition of endpoint

Plasma belantamab mafodotin (ADC, total mAb) and cys-mcMMAF concentration-time data will be analyzed by standard non-compartmental methods using WinNonlin, version 6.3 or later, as data permit.

- Pharmacokinetic parameters described in Table 4 below will be determined separately for each analyte, as data permit, for Cycle 1 and Cycle 3.
- The pharmacokinetic parameters C-EOI (end of infusion concentration) and Ctrough (concentration prior to dosing) will be determined directly from the concentration-time dataset for the other cycles. Note: For the dosing occasions with only pre-dose and end of infusion samples, the C-EOI will not be identified as Cmax.
- All calculations of non-compartmental parameters will be based on actual sampling times.

Table 4 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
Plasma belantamab mafodotin (ADC, total mAb) and cys-mcMMAF parameters	
AUC(0-t')	Area under the concentration-time curve to a fixed time t'
AUC(0-τ)	Area under the concentration-time curve during the dosing interval
Cmax	Maximum observed concentration, determined directly from the concentration-time data for each cycle. Cmax will not be derived when only predose and EOI samples were collected.
tmax	Time to reach Cmax, determined directly from the concentration-time data for each cycle
Cτ, Ctrough	Trough concentration prior to the next dose for each cycle
C-EOI	Observed plasma concentration at the end of infusion
tlast	Time of last observed quantifiable concentration

4.2.2. Main analytical approach

4.2.2.1. Concentration-Time Data

Linear and semi-logarithmic individual concentration-time profiles and mean and median profiles (by renal function group and cycle) will be plotted for belantamab mafodotin (ADC and total mAb) and cys-mcMMAF. Mean profiles may not be included in the analyses.

Concentrations of belantamab mafodotin (ADC and total mAb) and cys-mcMMAF will be listed for each participant and summarized (when appropriate) by planned time point, renal function group, cycle and matrix (e.g., plasma or dialysate as data permit).

4.2.2.2. Derived Pharmacokinetic Parameters

Primary plasma belantamab mafodotin (ADC, total mAb) and cys-mcMMAF PK parameters for Cmax, AUC(0-τ) and AUC(0-168h) will be analyzed on the log-scale using a linear regression model, including renal function group (normal or mildly impaired, severe, ESRD (not on dialysis), ESRD on (dialysis)) as a fixed effect. Cycle 1 and Cycle 3 data will be analyzed in separate models.

If a lower dose is used in Part 2 for the ESRD participants, the Cmax, AUC(0-τ) and AUC(0-168h) parameters will be dose normalized prior to analysis.

Dose normalization parameters will be calculated as:

Dose normalized parameter value = Parameter value *(2.5 / dose used in mg/kg).
Baseline covariates for gender, age, body weight, BMI, race, albumin, IgG and sBCMA will be investigated for inclusion into the models as deemed appropriate. If any covariates are included in the primary models, then a sensitivity analysis may be performed including only renal impairment group in the model, if appropriate. Dose normalized analyses will not be included in the Part 1 analyses and will be conditional displays for Part 2.

The geometric mean of each PK parameter will be derived from the models together with the ratio between the geometric means for the control group (normal or mildly impaired renal function) and each of the other renal function groups. The control group will be used as the denominator in all ratios so that an estimated ratio>1 will indicate that the relevant renal impairment group is estimated to have a higher value of the parameter of interest than the control group. 90% CIs will be included for the ratio between geometric means. A forest plot to compare the cys-mcMMAF PK parameters may be produced, presenting the ratio of geometric means of each renal function group vs the control group and the associated 90% Cis. This will be produced for Cycle 1, and Cycle 3 if data permit.

Distributional assumptions underlying each model used for analysis will be examined with a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality and constant variance assumptions of the model, respectively) to gain confidence that the model assumptions are reasonable.

If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data. If no alternative model is found to be reasonable then each renal-impaired group will be compared to the control group with a non-parametric Wilcoxon test.

Participants who did not provide sufficient PK samples to allow for the calculation of the PK parameters will not be included in the relevant models and no data imputation will be used to replace this missing data.

All derived PK parameters will be summarized by cycle, renal function group and matrix. Summaries of log-transformed parameters, including statistics for geometric mean, SD (on the log scale) and coefficient of variation, will also be produced by cycle, renal function group and matrix for all parameters except tmax and tlast.

Box plots by renal function group for plasma ADC, Total mAb and cys-mcMMAF PK parameters in Part 1 and dialysate PK parameters in Part 2 including Cmax, AUC(0-τ) and AUC(0-168h)(dose normalized if applicable) will be produced by cycle and analyte. The plots will present the Geometric mean and associated 90% CIs.

4.2.3. Supportive Analysis

Since participants were enrolled into the protocol defined renal function groups using eGFR (mL/min/1.73 m^2; standardized to body surface area (BSA) value of 1.73 m^2) pre-protocol amendment 2 and iGFR (eGFR converted back to mL/min) post-protocol amendment 2, a comparison plot will be provided to look for concordance. Individual eGFR will be plotted vs Standardized eGFR, both at screening, and lines will be included on both axes to indicate the category limits (i.e. 29 and 60).

4.3. Secondary Endpoint Analyses

Safety analysis will be based on the Safety analysis set by iGFR renal function group. A subset of key safety analyses will be displayed by eGFR as a sensitivity and will be defined in the OPS document. COVID-19 analyses (that are not covered by existing

standard Adverse Event displays) will be performed at final/primary analysis only and will be based on the COVID-19 analysis set.

4.3.1. Safety

4.3.1.1. Adverse Events

Adverse events summaries including the summary of adverse events (AEs), Serious AEs (SAEs) adverse events of special interest (AESIs) and other significant AEs will be based on GSK Core Data Standards.

An overview summary of AEs, including counts and percentages of participants with any AE, AEs related to study treatment, Grade 3, 4 and 5 AEs, Grade 3, 4 and 5 AEs related to study treatment, AEs leading to permanent discontinuation of study treatment, study treatment- related AEs leading to permanent discontinuation of study treatment, AE leading to dose reductions, AEs leading to dose interruptions and delays, SAEs, SAEs related to study treatment, fatal SAEs, and fatal SAEs related to study treatment will be produced. Unless otherwise specified, AEs will be summarized by renal function group.

'On treatment' for AEs is defined as from the start of treatment until 70 days after the last dose of study treatment, until the participant withdraws consent for study participation. Treatment Emergent for AEs is defined as time from first dose to last dose plus 70 days or start of new anti-cancer therapy, whichever comes first.

All AE tables will include treatment emergent AEs only, all AE listings will present all adverse events and will highlight AEs not on-treatment or treatment emergent.

Adverse events will be coded using the standard Medical Dictionary for Regulatory Affairs (MedDRA dictionary) and graded by the investigator according to the NCI-CTCAE, (version 5.0).

A summary of number and percentage of participants with any adverse events by maximum grade will be produced. AEs will be sorted by System Organ Class (SOC) and Preferred term (PT) in descending order. The summary will use the following algorithms for counting the participants:

- Preferred term row: Participants experiencing the same AE preferred term several times with different grades will only be counted once with the maximum grade.
- System organ class row: Each participant is counted only once at the maximum severity grade at each SOC level, although they may have several different preferred term events within the same SOC.
- Any event row: Each participant with at least one adverse event will be counted only once at the maximum grade no matter how many events they have.

The frequency and percentage of AEs (all grades) will be summarized and displayed in descending order by SOC and PT. A separate summary will be provided for study treatment -related AEs. A study treatment-related AE is defined as an AE for which the investigator classifies the possible relationship to study treatment as "Yes". 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. The summary table will be displayed by maximum grade sorted by PT in descending order. This table will be repeated for non-serious study treatment-related AEs.

All SAEs will be tabulated based on the number and percentage of participants who experienced the event and will be displayed by SOC, PT and maximum grade. Additionally, a table will be provided summarizing the number of occurrences as well as the number of participants with SAEs, the number of treatment-related SAEs, fatal SAEs and treatment-related fatal SAEs. This information will be provided for each SOC and PT.

A study intervention-related SAE is defined as an SAE for which the investigator classifies the relationship to study intervention as "Yes". A worst-case scenario approach will be taken to handle missing data, i.e. the summary table will include events with the relationship to study intervention as 'Yes' or missing.

A summary of non-serious AEs that occurred in 5% of the participants or above will be provided (no rounding for the percentage will be used in terms of 5% threshold, e.g., event with 4.9% incidence rate should not be included in this table). The summary will be displayed by SOC and PT.

Additional AE tables in descending order by PT will be provided for AEs leading to permanent discontinuation of study treatment, leading to dose reduction, and leading to dose interruption/delay. A summary of serious fatal and non-fatal study treatment AEs will also be provided by descending order of PT.

Finally, summaries of cumulative incidence of AEs as well as SAEs by number of doses received at first occurrence and PT will be provided. Preferred terms will be provided by descending frequency of any dose and the number of doses will be categorized based on the data.

All AEs will be listed. Additionally, a listing of participant IDs for each individual AE will be produced. Separate supportive listings with participant-level details will be generated for fatal and non-fatal SAEs, respectively. The relationship between MedDRA SOC, PT, and Verbatim Text will be listed.

4.3.1.2. Adverse Events of Special Interest

The following will be considered adverse events of special interest (AESI) for belantamab mafodotin for the purpose of analyses:

- Corneal adverse events
- Thrombocytopenia
- Infusion-related reactions [IRRs]

Adverse events of special interest will be identified based on a hybrid of terms identified in the eCRF and a list of terms identified from clinical review of all adverse event terms and graded using NCI- CTCAE (v5.0). Infusion-related reactions also consider if the adverse event is reported on the infusion day after the start of infusion, within 24 hours

following end of infusion and led to temporary interruption, prolongation of infusion time or treatment withdrawal.

Summaries of the number and percentage of participants with these events will be provided for each type of events separately by preferred term and maximum grade. The time of onset and duration of first occurrence of each type of events will be summarized using summary statistics mean, standard deviation, median, minimum value, and maximum. For corneal adverse events and thrombocytopenia, the time of onset will be derived from treatment start date to the first applicable AESI in days and the number and percentage of participants within each time category (1-21 days, 22-42 days, 43-63 days, >63 days) will be reported. Duration will also be derived from the start to the end of the AESI in days and the number and percentage of participants within each duration category (1-21 days, 22-42 days, >42 days) will be reported. The end of the AESI is defined as when the participant is free of any applicable events with at least 1 day gap before any other event of the same time occurs.

For the infusion-related reaction AESIs, the time of onset will be derived from the most recent infusion to the first applicable AESI in hours and the number and percentage of participants within each time category (0-6 hours, >6-12 hours, >12-18 hours, >18-24 hours, > 24 hours) will be reported. Duration will also be derived (from start to end of AESI) in hours and the number and percentage of participants within each duration category (0-12 hours, >12-24 hours, >24 hours) will be reported.

The summary of event characteristics will be provided for each AESI respectively, 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, number of occurrences (One, Two, Three or more), maximum grade, maximum grade for events related to study treatment, outcomes and the action taken for the event. The percentage will be calculated in two 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 maximum grade, i.e. a participant will only be counted once as the worst case from all the events experienced by the participant. Worst case will also be applied to outcome with the following hierarchy: Fatal> Not Recovered/Not Resolved> Recovered/Resolved with sequelae> Recovering/Resolving> Recovered/Resolved. For event characteristics and action taken to an event, a participant may be counted in more than one category, e.g. if a participant has an event leading to both study treatment discontinuation and dose reduction, the participants will be counted once under both actions.

4.3.1.3. COVID-19 Assessment and COVID-19 AEs

A standardized MedDRA Query (SMQ) will be used to identify all COVID-19 AEs. If there are any instances of COVID-19 the following summaries will be produced.

The overall incidence of AEs and SAEs of COVID-19 and COVID-19 AEs leading to study treatment discontinuation will be summarized. The incidence of these events at individual PT level can be obtained from the standard AE/SAE summaries.

COVID-19 assessments for participants with COVID-19 AEs will be summarized.

If >3 participants report ≥1 COVID-19 AE, then onset and duration of the first occurrence of COVID-19 AEs, and COVID-19 AE symptoms (from the COVID-19 eCRF page) will be summarized. The same rule will apply to COVID-19 SAEs.

4.3.1.4. Deaths

In the event that a participant has withdrawn consent, no data after the withdrawal of consent date from this participant including death is supposed to appear in the database.

All deaths will be summarized based on the number and percentage of participants. This summary will classify participants by time of death relative to the last dose of medication (>30 days or ≤30 days) and primary cause of death (disease under study, SAE related to study treatment, or other). A supportive listing will be generated to provide participant-specific details on participants who died including the primary cause of death.

4.3.1.5. Laboratory Data

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. Unless otherwise specified, the denominator in percentage calculation at each scheduled visit will be based on the number of participants with non-missing value at each particular visit.
Summary of change from baseline by scheduled visits using mean, median, standard deviation, minimum and maximum will be provided for hematology and chemistry.

Summaries of worst case grade increase from baseline grade will be provided for all the hematology and chemistry lab tests that are gradable by CTCAE v5.0. These summaries will display the number and percentage of participants with a maximum post-baseline grade increasing from their baseline grade. Any increase in grade from baseline will be summarized along with any increase to a maximum grade of 3 and any increase to a maximum grade of 4. 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 labelled by direction, e.g., sodium will be summarized as hyponatremia and hypernatremia separately.

For hematology and chemistry lab tests that are not gradable by CTCAE v5.0, 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 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.

For urinalysis tests, summaries of worst case changes from baseline will be generated. For urine occult blood dipstick, no change or decrease, any increase, increase to small, increase to moderate and increase to large will be summarized for the worst case post-baseline. For urine protein dipstick no change or decrease, any increase, increase to trace, increase to 1+, 2+, 3+ and 4+ will be summarized for the worst case post-baseline.

For spot urine albumin/creatinine ratio (mg/g), a shift table from baseline to worst post-baseline will be provided with the ratio categorized into <500, 500 – 2000 and >2000.

A supporting listing of hematology and chemistry laboratory data for participants with abnormalities of potential clinical concern, as well as a separate listing for urinalysis, will be provided. A separate listing of laboratory data with character values will also be provided.
Summaries of hepatobiliary laboratory events including possible Hy's law cases will be provided in addition to what has been described above. Possible Hy's law cases are defined as any elevated alanine aminotransferase (ALT) ≥3×upper limit of normal (ULN), total bilirubin≥2×ULN and alkaline phosphatase (ALP)<3×ULN/missing. 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. ALP<2×ULN/missing means it is satisfied unless the ALP is ≥2xULN at the time of bilirubin elevation. The summary will be produced for worst case post baseline only. Additionally, tables summarizing liver monitoring/stopping event reporting and liver restarts/re-challenges will be included along with listings of the recorded liver data. Data to be included will be participants meeting the hepatobiliary laboratory criteria post-baseline and liver monitoring/stopping event reporting. A liver event profile may be included.

4.3.1.6. Vital Signs

Values of vital signs (temperature, systolic and diastolic blood pressure, pulse rate) as well as the change from baseline will be summarized by timepoint and scheduled visit using mean, median, standard deviation, minimum and maximum. Weight may also be included.

In addition, summaries of grade increase in systolic blood pressure (SBP) and diastolic blood pressure (DBP) will be provided separately. These summaries will display the number and percentage of participants with any grade increase, increase to Grade 2 and increase to Grade 3 for worst case post-baseline only. The grade definition for SBP (mmHg) is: Grade 0 (<120), Grade 1 (120-139), Grade 2 (140-159), Grade 3 (≥160). The grade definition for DBP (mmHg) is: Grade 0 (<80), Grade 1 (80-89), Grade 2 (90-99), Grade 3 (≥100).

Additionally, a listing will be included for all vital sign data collected with grade included for SBP and DBP and L/H for pulse rate as applicable.

4.3.1.7. Ocular Assessments

Corneal Events identified and graded using the KVA scale will summarized. The overall KVA scale grade will be used from the CRF along with the relationship and action taken to study treatment associated with the event. The number and percentage of participants will be displayed by grade for the worst eye by visit.

A summary of event characteristics will be provided including number of participants with any event, number of participants with any event that is related to study treatment, maximum grade and the action taken for the event(s). The percentages will be calculated

in two ways, one with number of participants with event as the denominator and the other with total number of participants as the denominator. Participants may be included in more than one category for action taken.

A summary of the onset and duration of the first corneal event with KVA scale grade 2 or above will also be provided. The time of onset and duration of first occurrence will be summarized using summary statistics mean, standard deviation, median, minimum value, and maximum. The time of onset will be derived from treatment start date to the first event in days and the number and percentage of participants within each time category (1-21 days, 22-42 days, 43-63 days, >63 days) will be reported. Duration will also be derived (from start of the grade 2 event to the first time that KVA scale grade improves to grade 1 or better) in days and the number and percentage of participants within each duration category (1-21 days, 22-42 days, >42 days) will be reported.

Additional tables will summarize the number and percentage of participants within each action taken to study treatment by the maximum KVA scale grade experienced (across both eyes and visit) as well as the maximum KVA scale grade across both eyes by action taken and visit. A summary of cumulative incidence of corneal events (KVA scale) by number of doses received at first occurrence and grade will also be provided.

Finally, an overview of the corneal events (KVA scale) will provide the number and percentage of participants within the following categories (across both eyes): Any Event, Events related to study treatment, Grade 3 or 4 events, Grade 3 or 4 events related to study treatment, Events leading to permanent discontinuation of study treatment, Events related to study treatment and leading to permanent discontinuation, Events leading to dose reduction and Events leading to dose interruption/delay.

In addition to corneal events, best corrected visual acuity (BCVA) will be summarized based on the Logarithm of the Minimum Angle of Resolution (logMAR score) where:

$$\text{logMAR score} = -\log10(\text{Snellen Acuity Score}).$$

The logMAR score will be summarized using summary statistics mean, standard deviation, median, minimum value, and maximum for left, right, worst and better eye with the end of study visit and last follow-up exam. The number and percentage of participants will also be displayed within the categories “No change/improved vision” defined as a change from baseline <0.12, “Possible worsened vision” defined as a change from baseline >=0.12 to <0.3, “Definite worsened vision” defined as a change from baseline >=0.3, for left, right, worst and better eye within the end of study visit and last follow-up exam as well as maximum (worst) change from baseline and most frequent change from baseline.

For participants that have a Snellen Acuity response of “no equivalent value” will have a logMAR score result of 1000 to indicate a worsening in result when they have a corresponding non-Snellen Acuity response. These results will be included in the categorical summaries only.

Number and percentage of participants with a decline in BCVA to ‘light perception’ (LP) or ‘no light perception’ (NLP) anytime post-baseline will also be provided.

Supportive listings of visual acuity and abnormal corneal exam results as well as abnormal slit lamp lens exam results will be provided.

4.3.1.8. Performance Status

ECOG performance status will be summarized at baseline and each post-baseline scheduled visit. Summaries will use frequency and percentage of participants at each planned assessment time. A summary of change from baseline by scheduled visits will be performed, as well as the worst case post-baseline and the best-case post-baseline changes during the study (improved, no change, deteriorated). A supporting listing will also be provided.

4.4. Exploratory Endpoints Analyses

Exploratory analysis will be based on the PK evaluable analysis set unless otherwise specified. Listings may be produced on the PK analysis set as long as the PK evaluable analysis set is clearly identified.

4.4.1. Pharmacokinetics

The relationship between belantamab mafodotin and cys-mcMMAF PK parameters (e.g., Cmax, AUC) and baseline renal function parameters (e.g., standardized eGFR, individual eGFR etc) will be explored using scatter plots. Dialysis participants will be highlighted if data permits.

4.4.2. Cys-mcMMAF in Urine

From urine collection in Part 1 participants, the following will be listed: participant, timepoint, concentration, volume.

If data permit, summary tables will be produced by timepoint to examine Part 1 24-hour urine PK parameters (See Table 5) of cys-mcMMAF following the first dose.

Box plots by renal function group for Urine PK CLr if estimable may be produced. The plots will present the Geometric mean and associated 90% CIs.

Table 5 Derived Urine Pharmacokinetic Parameters

Urine PK parameters (Part 1 only)	
Ae(t1-t2)	Amount of drug excreted in urine in a 24- hour time intervals: C1D1, C1D4, C1D8, C1D15, and C1D21
Ae	Amount collected over the dosing interval
Fe(0-t)	Fraction of cys-mcMMAF dose excreted in urine (Ae/D)
CLr	Renal Clearance of cys-mcMMAF (if estimable, in mL/min calculated as Ae/AUC)

4.4.3. Anti-Drug Antibodies (ADAs)

For each participant, the anti-GSK2857916 (drug) antibody results, titers, and neutralizing antibody assay results, and also ADC and total antibody concentration will be listed for each assessment time point. The frequency and percentage of participants with positive and negative anti-drug antibody and neutralizing antibody assay results will be summarized for each assessment time and overall for each participant by dose cohort (data permitting) and will be listed. The conclusive results will be based on the total antibody concentration.

4.4.4. Tear Fluid

To evaluate the presence of belantamab mafodotin and free cys-mcMMAF in tear fluid in participants with normal/mildly impaired or severely impaired renal function (Part 1 only), the presence of belantamab mafodotin and cys-mcMMAF in tear fluid at baseline and on treatment will be summarized by timepoint (data permitting) and listed.

4.4.5. ECG and Echocardiograms (ECHO)

Post baseline ECGs and ECHOs are only to be performed when clinically indicated. All ECG and ECHO data will therefore only be listed. Abnormal finding and all values will be listed for ECGs on the Safety analysis set. The QTc values based on Fridericia formula (QTcF) will be rounded to the integer and the values will be categorized into the following CTCAE grade and ranges: Grade 0 (<450 msec), Grade 1 (450-480 msec), Grade 2 (481-500 msec), and Grade 3 (≥501 msec). The left ventricular ejection fraction will be listed for ECHO on the Safety analysis set.

4.4.6. Efficacy

The exploratory efficacy endpoints for this study include Overall Response Rate (ORR), Clinical Benefit Rate (CBR), Duration of Response (DoR), Time to Response (TTR) and Time to Progression (TTP). No hypothesis testing will be performed on these endpoints. Efficacy analysis will be based on the Safety Analysis Set.

Confirmation of response is defined in Table 6. In this study, censoring rules are tailored for DoR, and TTP endpoints (see Table 7), due to the limited sample size and follow-up.

Table 6 Response confirmation algorithm based on visit-level response

#	Response at the First Time Point	Response at Subsequent Disease Assessment[1]	Confirmed Response at the First Time Point
1	sCR	sCR	sCR
2	sCR	CR	CR
3	CR	sCR/CR	
4	sCR/CR	VGPR	VGPR
5	VGPR	sCR/CR/VGPR	
6	sCR/CR/VGPR	PR	PR
7	PR	sCR/CR/VGPR/PR	
8	sCR/CR/VGPR/PR	MR	MR
9	MR	sCR/CR/VGPR/PR/MR	
10	sCR/CR/VGPR/PR/MR	SD	SD
11	sCR/CR/VGPR/PR/MR	PD (any reason) OR No subsequent disease assessment: participant **died or discontinued study or started new anti-cancer therapy** before further adequate disease assessment	SD
12	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 No subsequent disease assessment: participant **died due to PD** before further adequate disease assessment (including death due to PD after initiation of new anti-cancer therapy)	PD
13	PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion)	sCR/CR/VGPR/PR/MR/SD OR No subsequent disease assessment: participant died **due to reasons other than PD** before further adequate disease assessment OR No subsequent disease assessment: participant **discontinued study** before further adequate disease assessment	NE
14	sCR/CR/VGPR/PR/MR/PD (due to reasons other than	No subsequent disease assessment: participant has	Unconfirmed sCR/CR/VGPR/PR/MR/PD.

#	Response at the First Time Point	Response at Subsequent Disease Assessment[1]	Confirmed Response at the First Time Point
	imaging, i.e., plasmacytoma or bone lesion)	not died, discontinued from study or (except for PD) started new anti-cancer therapy; but as yet has no further adequate disease assessments	Will be categorized as NE for final ORR analysis.
15	SD	Any OR No subsequent disease assessment	SD
16	PD due to imaging (plasmacytoma or bone lesion)	Any OR No subsequent disease assessment	PD
17	NE or missing	Any OR No subsequent disease assessment	NE

1. Subsequent disease assessment is defined as the next adequate (not missing or NE) disease assessment following the first timepoint 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 PD after new anti-cancer therapy are considered for confirmation of PD. No minimal time interval is required for the subsequent disease assessment, but a different sample is required for confirmation.
2. SD does not need to be confirmed.
3. PD due to imaging (i.e., plasmacytoma or bone lesion) does not need to be confirmed.
4. Where criteria are not mutually exclusive, take the first that applies.

Table 7 Assignments for Progression and Censoring Dates for TTP Analysis

Situation	Date of Event (Progression/Death) or Censoring	Outcome Event (progression/Death) Or Censored
No *(or inadequate)* baseline tumor assessments [1] and the participant has not died (if the participant has died follow the rules for death indicated at the bottom of the table)	Treatment start date	Censored
No post-baseline assessments and the participant has not died (if the participant has died follow the rules	Treatment start date	Censored

Situation	Date of Event (Progression/Death) or Censoring	Outcome Event (progression/Death) Or Censored
for death indicated at the bottom of the table)		
Progression documented at or between scheduled visits, without extended loss-to-follow-up time [4]	Date of assessment of progression	Event
No progression *(or death)*	Date of last 'adequate' assessment of response [2]	Censored
New anticancer treatment started *(prior to documented disease progression or death)* [3]*.*	Date of last 'adequate' assessment of response [2] *(on or prior to starting anti-cancer therapy)*	Censored
Death due to progression without extended loss-to-follow-up time [4]	Date of death	Event
Death from causes other than progression without extended loss-to-follow-up time [4]	Date of death	Censored *(Event for DOR2)*
Death or progression after an extended loss-to-follow-up time [4]	Date of last 'adequate' assessment of response [2] prior to PD/death *(prior to missed assessments)*	Censored
Death or progression after an extended loss-to-follow-up time [4] from treatment start date	Treatment start date	Censored

[1]. Adequate baseline assessment is defined as at baseline, a patient has at least one of the following measurements: a. Serum M-protein ≥0.5 g/dL (≥5 g/L) or b. Urine M-protein ≥200 mg/24h or c. Serum FLC assay: Involved FLC level ≥10 mg/dL (≥100 mg/L) and an abnormal serum free light chain ratio (<0.26 or >1.65)

[2]. An adequate assessment is defined as an assessment where the derived/Investigator determined response is sCR, CR, VGPR, PR, MR, or SD.

[3]. If PD or death and New anti-cancer therapy occur on the same day assume the progression or death was documented first (e.g., outcome is progression or death and the date is the date of the assessment of progression or death). If anti-cancer therapy is started prior to any adequate assessments, censoring date should be the date of first dose of study treatment.

[4]. Extended loss-to-follow-up time = 6 weeks + 7 day window = 49 day window; Without extended loss-to-follow-up time is defined as: <= 49 days; after an extended loss-to-follow-up time is defined as: >49 days.

4.4.6.1. ORR (Overall Response Rate)

ORR is defined as the percentage of participants with a confirmed Partial Response (PR) or better (i.e., PR, Very Good PR (VGPR), Complete Response (CR) and stringent Complete Response (sCR), according to the IMWG Response Criteria [Kumar, 2016], A participant with best confirmed response of PR or better (sCR+CR+VGPR+PR) will be considered as a responder for ORR. Participants with unknown or missing response will be treated as non-responders; i.e., these participants will be included in the denominator when calculating percentages of response.
The ORR and corresponding 95% exact CI will be summarized by renal function group. A supportive summary of best response by renal function group will also be produced. Additionally, a profile plot by renal function group will be provided, summarizing individual participant duration of exposure, time of best response, time of first response (of PR or better) and time of confirmed PD.

4.4.6.2. CBR (Clinical Benefit Rate)

CBR is defined as the percentage of participants with a confirmed minimal response (MR) or better (i.e., MR, PR, VGPR, CR, and sCR), according to the IMWG Response Criteria [Kumar, 2016].
CBR will be summarized in the same way as ORR.

4.4.6.3. DoR (Duration of Response)

There are two definitions of DoR to be considered.

- Definition 1: DoR until earliest date of disease progression (PD) or death due to PD
- Definition 2 (Sensitivity analysis): DoR until earliest date of disease progression (PD) or death due to any causes

For definition 1, DoR is defined as the time in months from first documented evidence of PR or better until the earliest date of disease progression (PD) per IMWG or death due to PD among participants who achieve a response (i.e. confirmed PR or better). Details of censoring rules can be found from Table 7. Participants who have not progressed or died due to PD prior to the end of the relevant reporting effort will be censored at the end of the reporting period. Participants who die from causes other than progressive disease will be censored at their date of death.

For definition 2, DoR is defined as the time in months from first documented evidence of PR or better until the earliest date of PD per IMWG or death due to any cause among participants who achieve a response (i.e. confirmed PR or better). Censoring rules from Table 7 can be followed except for participants who die due to any cause. Participants who have not progressed or died due to any cause prior to the end of the relevant reporting effort will be censored at the end of the reporting period.

If data permit, distribution of DoR for both definitions will be summarized using the Kaplan-Meier method by renal function group. The median, 25th and 75th percentiles of DoR will be estimated and corresponding 95% confidence intervals will be estimated

using the Brookmeyer-Crowley method (1982). Kaplan-Meier Plots by renal function group will be produced, if data permit.

In addition, descriptive statistics will be provided for the following:

- Participants who achieve PR or better until earliest PD or death due to PD
- Participants who achieve PR or better until earliest PD or death due to any cause.

4.4.6.4. TTR (Time to Response)

TTR is defined as the time between the start date of treatment and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better).

For TTR, descriptive statistics will be provided for participants who achieve PR or better.

4.4.6.5. TTP (Time to Progression)

TTP is defined as the time from start date of treatment until the earliest date of PD or death due to PD per IMWG. Determination of dates of TTP event and dates for censoring are described in Table 7.

If data permit, distribution of TTP will be summarized using the Kaplan-Meier method by renal function group. The median, 25th and 75th percentiles of TTP will be estimated and corresponding 95% confidence intervals will be estimated using the Brookmeyer-Crowley method (1982). Kaplan-Meier Plots by renal function group will be produced, if data permit. Otherwise, descriptive statistics will be provided for participants with PD or death due to PD.

4.5. Other Analyses

The other analyses will be based on the Safety Analysis Set, unless otherwise specified. Outputs will be displayed by iGFR categories but some outputs may be repeated by eGFR as a sensitivity.

4.5.1. Extent of Exposure

Extent of exposure to belantamab mafodotin will be summarized. The number of cycles administered to study treatment will be summarized with mean, median, standard deviation, minimum, and maximum. The dose intensity (mg/kg/3 weeks), which is calculated as the cumulative actual dose (mg/kg) divided by expected duration of exposure in 3 weeks [(last infusion date – first infusion date+21)/21], will also be summarized. A by participant summary listing of data on exposure to will be produced.

The duration of exposure to study treatment [minimum of (last dose of study treatment + 20 days, death date, date of cut off, last contact date for discontinued subjects) – Start date of study treatment + 1] will be calculated in weeks and summarized using mean, median, standard deviation, minimum, and maximum. A horizontal bar graph of duration of treatment will be produced that displays duration of treatment in weeks for each participant.

Dose delivered by cycle (mg/kg/cycle) will be summarized using mean, median, standard deviation, minimum, and maximum by cycle and overall.

Dose reductions and delays will be summarized separately for the number of reductions/delays, reasons for reductions/delays and number of participants with dose reductions/delays by planned time. The duration will also be included for dose delays (days) and the number and percentage of the delays for intervals of 1-21, 22-42 and >42 days will be computed. Primary reasons for dose reductions and dose delays will also be summarized by cycle.

A plot showing the number and percentage of participants at each actual dose level (mg/kg) received, including dose reductions, by cycle will be provided. Supportive listings for dose reduction and delays will also be provided.

4.5.2. Population Pharmacokinetic (PopPK) Analyses

Plasma belantamab mafodotin concentration-time data may be combined with data from other studies and analyzed using a population pharmacokinetic approach. The initial analysis will use the population pharmacokinetic model developed for Study BMA117159 and Study 205678 to generate post hoc pharmacokinetic parameter. Details of these analyses will be reported under a separate SAP and results may be provided in a separate report.

4.5.3. Pharmacokinetic / Pharmacodynamic Analyses

If deemed appropriate and if data permit, exposure-response relationships between belantamab mafodotin exposure (e.g., dose, dose intensity, concentration, Cmax, or AUC) and clinical activity and/or toxicity (e.g., response, corneal event, AESIs) may be explored using population methods. If data permit, the effects of covariates may be explored.
Details of these analyses will be reported under a separate SAP, and the results of this analysis will be provided in a separate report.

4.5.4. Pharmacodynamic and Biomarker Analyses

If data permit, actual change and percent change of free BCMA expression level from baseline will be summarized using descriptive statistics (mean, SD, median, min, max) and displayed using boxplot by visit and time. If data permit, additional analyses will be specified within a separate biomarker SAP, e.g. circulating free DNA assessments at baseline, during response, and end of treatment will be explored; the relationship between clinical response and other biologic characteristics including BCMA expression on tumour cells and sBCMA concentrations may be explored. If warranted, the results of these additional analysis will be provided in a separate report.

5. SAMPLE SIZE DETERMINATION

Thirty-two (32) to 36 participants will be targeted for PK analysis for this study. It is estimated that approximately 100 participants need to be screened, and up to 36 participants to be enrolled. The study is composed of two parts that include up to 12 participants with normal or mildly impaired renal function and 8 with severe renal impairment for Part 1, and up to 8 participants with ESRD (not on dialysis) and up to 8 participants with ESRD (on dialysis) for Part 2.

The above targeted sample size was chosen based on feasibility, to address the objectives of the study. This sample size is considered sufficient to determine whether the pharmacokinetics in participants with renal impairment is meaningfully different from participants with normal renal function.

For Cmax and AUC[0-168h] of cys-mcMMAF, the variance of the natural log-transformed data is 0.224 and 0.245 respectively (estimated from Study BMA117159). Assuming variance of 0.245 and 8 participants with normal renal function and 8 participants with severe renal impairment will be evaluable for PK analysis in Part 1, the estimated distribution of observed ratio between sample mean ([R_obs]: severe vs. normal) of Cmax or AUC0-168h are shown in Table 8.

Table 8 Estimated Distribution of Observed Ratio for cys-mcMMAF Cmax or AUC[0-168h]

True Ratio	Observed Ratio Severe Renal Impairment vs. Normal Renal Function)		
Severe vs. Normal	Probability (%)		
	(R_obs≤1.25)	(1.25<R_obs≤1.5)	(R_obs>1.5)
1.00	81.6	13.3	5.1
1.05	75.9	16.6	7.5
1.10	69.7	19.8	10.5
1.15	63.2	22.7	14.2
1.20	56.6	25.1	18.4
1.25	50.0	26.9	23.1
1.30	43.7	28.1	28.2
1.35	37.8	28.7	33.5
1.40	32.4	28.6	39.0
1.45	27.4	28.0	44.6
1.50	23.1	26.9	50.0
1.60	15.9	23.8	60.3
1.70	10.7	19.9	69.3
1.80	7.0	16.0	76.9
1.90	4.5	12.4	83.0
2.00	2.9	9.4	87.7

Note: Probabilities were calculated assuming natural log of cys-mcMMAF Cmax or AUC0-168h follows normal distribution with a variance of 0.245.

As shown in the above table, if the true ratio (severe vs normal) for a parameter is 1.0 (i.e., no difference), there is more than 80% (81.6%) chance that the observed ratio from Part 1 of the study will be less than 1.25; if the true ratio (severe vs normal) is 1.5 (i.e., significant difference), there is <25% (23.1%) chance observed parameter ratio from Part 1 study will be <1.25.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 Study Population Analyses

Unless otherwise specified, the study population analyses in this section will be based on the Safety Analysis Set and displayed by iGFR categories. A summary of the number of participants in each of the participant level analysis set will be provided along with a listing of participants excluded from analysis sets on the Enrolled Analysis Set.

6.1.1. Participant Disposition

A summary of the number and percentage of participants who completed the study as well as those who prematurely withdrew from the study or who are ongoing on study treatment or in follow up will be provided on the Enrolled Analysis Set. A listing of reason for study withdrawal will also be provided with the additional responses for lost to follow-up included.

A summary of study treatment status will also be provided. This display will show the number and percentage of participants who have completed the scheduled study treatment, are ongoing with study treatment, or have discontinued study treatment, as well as primary reasons for discontinuation of study treatment. A listing of study treatment discontinuation will be provided with last dose date, date of decision to receive no future study treatment and additional specified reasons for study treatment discontinuation included.

A summary table and listing identifying reasons for screening failures will be presented based on the Screened Analysis Set.

Duration of follow-up in months, defined as the time from treatment start to last contact or death, will be summarized by minimum, median, maximum and first and third quartiles.

6.1.2. Demographic and Baseline Characteristics

The demographic characteristics including age, sex, ethnicity, height/weight/BMI at screening and race will be summarized with descriptive statistics. In addition, age will also be categorized and summarized by 18-64, 65-84, and ≥85 years for the Enrolled Analysis Set for compliance with Regulatory requirements as well as part of the demography summary table. Race and racial combinations will also be listed.

Disease characteristics at screening, including stage, type of multiple myeloma, myeloma light chain and myeloma immunoglobulin, extramedullary disease, lytic bone lesion, lines of prior therapy and genetic characteristics (including high cytogenetic risk) will be summarized and listed. Both the eGFR standardized by BSA and individualized GFR will also be included as a continuous value and categorized as <15, 15-29, 30-59, 60-89, ≥90.

Disease characteristics at initial diagnosis will be summarized and listed separately and will include time since initial diagnosis in years, date of initial diagnosis (listing only) and stage at initial diagnosis.Past medical conditions and current medical conditions as of screening will be summarized respectively.

Ocular history and risk factors including will be summarized, including previous diagnosis of dry eye, history or glaucoma, cataract, history of ocular surgeries, serious eye trauma, ocular disease requiring medical treatment, diabetic retinopathy, macular degeneration, macular edema and whether a participant is taking any topical eye treatment.

Substance use, including smoking history, tobacco use, alcohol and drug history will be summarized.

6.1.3. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarized and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the current version of the Protocol Deviation Management Plan. These protocol deviations will be reviewed to identify those considered as important as follows:

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorized in the protocol deviations dataset.
- This dataset will be the basis for the summaries of important protocol deviations.

In addition to the overall summary of important protocol deviations, separate summaries will be produced for important protocol deviations related to COVID-19, and important protocol deviations not related to COVID-19 respectively.

A separate listing of all inclusion/exclusion criteria deviations will also be provided for the Safety Population. This will be based on data as recorded on the inclusion/exclusion page of the eCRF.

6.1.4. Prior and Concomitant Medications

Concomitant medications will be coded using both the GSK Drug and WHO Drug dictionaries. However, the summary will be based on GSK Drug dictionary only. The summary of concomitant medications will be provided by ingredient, i.e. multi-ingredient medications will be summarized for each individual ingredient rather than a combination of ingredients. The summary will be created using ingredient base names, i.e. ingredients with the same base name but different salt will appear under one base name in the summary. Anatomical Therapeutic Chemical (ATC) classifications will not appear in the summary.

A separate listing of all concomitant medications by ATC level, ingredient and verbatim text will also be provided.

Summary of Concomitant Medications: This summary will contain medications (general medications) including those with start date prior to study treatment start date and continue (missing end date or end date after study treatment start date) on therapy. Note that any medications with start date and end date prior to study treatment start date will be excluded. Include concomitant medication records where start relative to treatment in ('BEFORE','DURING') and end relative to treatment in ('DURING','AFTER').

Prophylactic medication for infusion related reactions will be summarized by drug class and name with a supportive listing.

Prior anti-cancer therapy will be summarized by type of therapy, and drug class. Follow-up anti-cancer therapies will also be summarized by type of therapy as well as including the time from study treatment discontinuation to the first post-study treatment anti-cancer therapy. Supportive listings for prior and follow-up anti-cancer therapies will be provided along with listings for anti-cancer radiotherapy and prior & post treatment cancer and non-cancer related surgical procedures.

Blood products or blood supportive care products with onset date within the on-treatment window will be included in the summary tables. The number and percentage of participants using blood products and blood supportive care products after the start of study treatment will be provided. Supporting listings will also be provided.

6.1.5. Additional Analyses Due to the COVID-19 Pandemic

A participant is defined as having a suspected, probable or confirmed COVID-19 infection during the study if the answer is “Confirmed”, “Probable” or “Suspected” to the case diagnosis question from the COVID-19 coronavirus infection assessment eCRF. Numbers of participants with a suspected, probable or confirmed COVID-19 infection, and of COVID-19 test results will be summarized.

Additionally, if greater than 5 participants have a suspected, probable of confirmed COVID-19 infection, the following data displays will be produced:

- Summary of current medical conditions for participants with COVID-19 adverse events.
- Summary of baseline characteristics for participants with COVID-19 adverse events.

6.2. Appendix 2 Data Derivations Rule

6.2.1. Criteria for Potential Clinical Importance

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.

National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v5.0) will be used to assign grades to the relevant laboratory parameters and blood pressure.

For laboratory data which are not listed in the NCI CTCAE v5.0, a summary of values outside the normal range will be provided.

In addition, the following criteria will be used to flag potential clinical importance:

Parameters	Unit	PCI Range
Heart rate	bpm	<60 (L); >100 (H)

6.2.2. Study Period

Assessments and events will be classified according to the time of occurrence relative to the study treatment period.

Pre-Treatment is defined as time prior to the first dose of study treatment.

On-Treatment is defined as time from first dose to last dose date plus 70 days.

For assessment or event on the first dosing day, whether it is Pre-Treatment or On-Treatment should be based on time if available. If time is not available, the first dosing day (Day 1) is considered Pre-Treatment for ECOG, ECG, vital signs, lab tests, cardiac scan, and other safety domains, and On-Treatment for adverse events, liver events and concomitant medications.

Post-Treatment is defined as any time post on-treatment window, i.e. > last dose date + 70 days.

6.2.2.1. Treatment Emergent Flag for Adverse Events

Treatment Emergent is defined as the time from first dose to last dose plus 70 days or start of new anti-cancer therapy, whichever comes first. If time of AE or study treatment is not collected, AEs starting on the first dose date will be considered treatment emergent. If start date is missing the AE will be considered treatment emergent.

6.2.3. Multiple measurements at One Analysis Time Point

For lab tests on a study day, if more than one assessment is taken on the same day, the test from a central lab will be taken over the test from a local lab. If multiple assessments are taken from the same type of lab, the worst case will be used.

6.3. Appendix 3 List of Data Displays for Combined Safety/PK Interim Analysis

6.3.1. Study Population Tables

Study Population Tables: Total number of Safety Population Tables		
Population	**GSK Standard / Example Shell**	**Title**
ENRLFL	CCI	Summary of Subject Status and Subject Disposition for the Study Conclusion Record
SAFFL		Summary of Treatment Status and Reasons for Discontinuation of Study Treatment
Protocol Deviation		
SAFFL	CCI	Summary of Important Protocol Deviations
Demographic and Baseline Characteristics		
SAFFL	CCI	Summary of Demographic Characteristics
SAFFL		Summary of Disease Characteristics at Screening
Prior and Concomitant Medications		
SAFFL	CCI	Summary of Concomitant Medications
Prior and Follow-up Anti-Cancer Therapy		
SAFFL	CCI	Summary of Prior Anti-Cancer Therapy by Drug Class of Agents
Duration of Follow-up		
SAFFL	CCI	Summary of Duration of Follow-Up

6.3.2. Efficacy Tables

Efficacy Tables: Total number of Efficacy Tables		
Population	**GSK Standard / Example Shell**	**Title**
Response		
SAFFL	CCI	Summary of Investigator Assessed Best Response with Confirmation (IMWG 2016 Criteria)

Efficacy Tables: Total number of Efficacy Tables		
Population	**GSK Standard / Example Shell**	**Title**
Time to Event		
SAFFL	CCI	Summary of Duration of Response 1 Based on Investigator-Assessed Response with Confirmation
SAFFL		Summary of Duration of Response 2 Based on Investigator-Assessed Response with Confirmation
SAFFL		Summary of Duration of Response 1 Based on Investigator-Assessed Response with Confirmation for Participants who Progress or Death is Due to PD
SAFFL		Summary of Duration of Response 2 Based on Investigator-Assessed Response with Confirmation for Participants who Progress or with Death due to any Cause
SAFFL		Summary of Time to Response Based on Investigator-Assessed Response with Confirmation
SAFFL		Summary of Time to Progression Based on Investigator-Assessed Response with Confirmation

6.3.3. Efficacy Figures

Efficacy Figures: Total number of Efficacy Figures		
Population	**GSK Standard / Example Shell**	**Title**
Response		
SAFFL		Profile Plot for Subjects
Time to Event		
SAFFL	CCI	Graph of Kaplan Meier Curves of Duration of Response 1 Based on Investigator-Assessed Response
SAFFL		Graph of Kaplan Meier Curves of Duration of Response 2 Based on Investigator-Assessed Response
SAFFL		Graph of Kaplan Meier Curves of Time to Progression Based on Investigator-Assessed Response

6.3.4. Safety Tables

Safety Tables: Total number of Safety Tables		
Population	**GSK Standard / Example Shell**	**Title**
Exposure		
SAFFL	CCI	Summary of Exposure to Belantamab Mafodotin
SAFFL		Summary of Exposure to Belantamab Mafodotin (eGFR sensitivity analysis)
Adverse Events (AEs)		
SAFFL	CCI	Adverse Event Overview
SAFFL		Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade
SAFFL		Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade (eGFR sensitivity analysis)
AEs of Special Interest		
SAFFL	CCI	Summary of Characteristics of Thrombocytopenia
SAFFL		Summary of Characteristics of Thrombocytopenia (eGFR sensitivity analysis)
SAFFL		Summary of Onset and Duration of the First Occurrence of Thrombocytopenia
SAFFL		Summary of Onset and Duration of the First Occurrence of Thrombocytopenia (eGFR sensitivity analysis)
SAFFL		Summary of Thrombocytopenia and Bleeding Event
SAFFL		Summary of Thrombocytopenia and Bleeding Event (eGFR sensitivity analysis)
SAFFL		Summary of Characteristics of Infusion-Related Reactions
SAFFL		Summary of Characteristics of Infusion-Related Reactions (eGFR sensitivity analysis)
SAFFL		Summary of Onset and Duration of the First Occurrence of Infusion-Related Reactions
SAFFL		Summary of Onset and Duration of the First Occurrence of Infusion-Related Reactions (eGFR sensitivity analysis)
SAFFL		Summary of Characteristics of Corneal Events (CTCAE Grade)
SAFFL		Summary of Characteristics of Corneal Events (CTCAE Grade) (eGFR sensitivity analysis)
SAFFL		Summary of Onset and Duration of the First Occurrence of Corneal

Safety Tables: Total number of Safety Tables		
Population	**GSK Standard / Example Shell**	**Title**
	CCI	Events (CTCAE Grade)
SAFFL		Summary of Onset and Duration of the First Occurrence of Corneal Events (CTCAE Grade) (eGFR sensitivity analysis)
Death		
SAFFL	CCI	Summary of Deaths
Serious and Other Significant Adverse Events		
SAFFL	CCI	Summary of Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade
SAFFL		Summary of Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade (eGFR sensitivity analysis)
SAFFL		Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment by Preferred Term
Corneal Events		
SAFFL	CCI	Summary of Characteristics of Corneal Events (KVA Scale)
SAFFL		Summary of Characteristics of Corneal Events (KVA Scale) (eGFR sensitivity analysis)
SAFFL		Summary of Onset and Duration of the First Occurrence of Corneal Events (KVA Scale) of Grade 2 or Above
SAFFL		Summary of Onset and Duration of the First Occurrence of Corneal Events (KVA Scale) of Grade 2 or Above (eGFR sensitivity analysis)
Laboratory: Chemistry		
SAFFL	CCI	Summary of Worst Case Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline
SAFFL		Summary of Worst Case Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline
Laboratory: Hepatobiliary (Liver)		
SAFFL	CCI	Summary of Hepatobiliary Laboratory Abnormalities
Vital Signs		
SAFFL	CCI	Summary of Change from Baseline in Vital Signs

6.3.5. Pharmacokinetic Tables

Pharmacokinetic Tables: Total number of Pharmacokinetic Tables		
Population	**GSK Standard / Example Shell**	**Title**
Concentration		
PKEFL	CCI [redacted]	Summary of Plasma GSK2857916 (ADC) PK Concentration-Time Data by Renal Function Group
PKEFL		Summary of Plasma GSK2857916 (Total Antibody) PK Concentration-Time Data by Renal Function Group
PKEFL		Summary of Plasma cys-mcMMAF PK Concentration-Time Data by Renal Function Group
PKEFL		Summary of Urine cys-mcMMAF PK Concentration-Time Data by Renal Function Group
PK Parameter		
PKEFL	CCI [redacted]	Summary of Derived Plasma GSK2857916 (ADC) PK Parameters by Renal Function Group
PKEFL		Summary of Derived Plasma GSK2857916 (Total Antibody) PK Parameters by Renal Function Group
PKEFL		Summary of Derived Plasma cys-mcMMAF PK Parameters by Renal Function Group
PKEFL		Summary of Derived Urine cys-mcMMAF PK Parameters by Renal Function Group
PKEFL		Analysis of Derived Plasma GSK2857916 (ADC, Total Antibody, cys-mcMMAF) PK Parameters by Cycle

6.3.6. Pharmacokinetic Figures

Pharmacokinetic Figures: Total number of Pharmacokinetic Figures		
Population	**GSK Standard / Example Shell**	**Title**
Concentration		
PKEFL	CCI [redacted]	Median Plasma GSK2857916 (ADC) Concentration-Time Plots (Linear and Semi-Log)
PKEFL		Median Plasma GSK2857916 (Total Anti-body) Concentration-Time Plots (Linear and Semi-Log)
PKEFL		Median Plasma GSK2857916 (cys-mcMMAF) Concentration-Time Plots (Linear and Semi-Log)
Parameters		
PKEFL	CCI [redacted]	Plot of Individual (+Geometric Mean and 90% CI) Plasma GSK2857916 Cmax vs Cycle by Renal Function Group and Analyte (ADC, Total Antibody and cys-mcMMAF)
PKEFL		Plot of Individual (+Geometric Mean and 90% CI) Plasma GSK2857916 (ADC) AUC vs Cycle by Renal Function Group and Analyte (ADC, Total Antibody and cys-mcMMAF)
PKEFL		Forest Plot to Compare cys-mcMMAF Pharmacokinetic Parameters

6.3.7. ICH Listings

ICH Listings: Total number of ICH Listings		
Population	**GSK Standard / Example Shell**	**Title**
Population Analysed		
ENRFL	CCI	Listing of Subjects Excluded from Any Population
Demographic and Baseline Characteristics		
SAFFL	CCI	Listing of Demographic Characteristics
Protocol Deviations		
SAFFL	CCI	Listing of Important Protocol Deviations
Exposure and Treatment Compliance		
SAFFL	CCI	Listing of Exposure to Belantamab Mafodotin
SAFFL		Listing of Dose Reductions of Belantamab Mafodotin
SAFFL		Listing of Dose Delays of Belantamab Mafodotin
Adverse Events		
SAFFL	CCI	Listing of All Adverse Events

Pharmacokinetic		
PKFL	CCI [redacted]	Listing of Plasma GSK2857916 (ADC) PK Concentration-Time Data
PKFL		Listing of Plasma GSK2857916 (Total Antibody) PK Concentration-Time Data
PKFL		Listing of Plasma cys-mcMMAF PK Concentration-Time Data
PKFL		Listing of Derived Plasma GSK2857916 (ADC) PK Parameters (Untransformed)
PKFL		Listing of Derived Plasma GSK2857916 (Total Antibody) PK Parameters (Untransformed)
PKFL		Listing of Derived Plasma cys-mcMMAF PK Parameters (Untransformed)
PKFL		Listing of Derived Urine cys-mcMMAF PK Parameters (Untransformed)

7. ABBREVIATIONS AND TRADEMARKS

7.1. List of Abbreviations

Abbreviation	Description
ADA	Anti-drug antibodies
ADC	Antibody-drug conjugate
AE	Adverse event
AESI	Adverse events of special interest
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the curve
BSA	Body surface area
CBR	Clinical Benefit Rate
C-EOI	Concentration at end of infusion
CI	Confidence interval
CL	Clearance
CLD	Dialysis clearance
Cmax	Maximum observed concentration
CR	Complete Response
CRF	Case report form
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
Ctrough	Predose plasma concentration
DBP	Diastolic blood pressure
DoR	Duration of Response
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eGFR	Estimated glomerular filtration rate
ESRD	End stage renal disease
FDA	Food and Drug Administration
GSK	GlaxoSmithKline
ICF	Informed Consent Form
iGFR	Individual glomerular filtration rate
IRR	Infusion-related reaction
IV	Intravenous
KVA	Keratopathy Visual Acuity
mAb	Monoclonal antibody
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
ORR	Overall Response Rate
OPS	Output and Programming Specification
PCI	Potential clinical importance
PD	Progressive Disease
PK	Pharmacokinetics

Abbreviation	Description
PopPK	Population Pharmacokinetic
PR	Partial Response
PT	Preferred term
Q3W	Once every 3 weeks
QTc	Corrected QT interval (ECG)
QTcF	Corrected QT interval Fridericia
RRMM	Relapsed / refractory multiple myeloma
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBP	Systolic blood pressure
sCR	Stringent Complete Response
SD	Stable Disease
SDTM	Source data tabulation model
SOC	System organ class
SOI	Start of Infusion
tlast	Last time point where the concentration is above the limit of quantification
tmax	Time of maximum observed concentration
TTP	Time to Progression
TTR	Time to Response
ULN	Upper limit of normal
VGPR	Very Good Partial Response

7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
MedDRA
NONMEM
SAS
WinNonlin

8. REFERENCES

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics, 1982; 38:29-41.

FDA DHHS; Department of Health and Human Services. Draft Guidance: Guidance for Industry Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing (fda.gov). September 2020; Revision 2. (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM204959.pdf.)

Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, Kusek JW, Van Lente F; Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006 Aug 15;145(4):247-54. doi: 10.7326/0003-4819-145-4-200608150-00004. Erratum in: Ann Intern Med. 2008 Oct 7;149(7):519. Erratum in: Ann Intern Med. 2021 Apr;174(4):584. PMID: 16908915.

Kumar S, Paiva B, Anderson KC, Durie B, Landgren O, Moreau P, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. The Lancet Oncology. 2016;17: e328-46

Mosteller RD, 1987, Simplified Calculation of Body Surface Area, N Engl J Med, 317:1098.