STATISTICAL ANALYSIS PLAN – AMENDMENT 3

AND

STATISTICAL ANALYSIS PLAN – ADDENDUM

Sponsor:	Genmab
Protocol Title:	First-in-human, open-label, dose-escalation trial with expansion cohorts to evaluate safety of Axl-specific antibody-drug conjugate (enapotamab vedotin, HuMax®-AXL-ADC) in subjects with solid tumors
Protocol Versions:	Final version 10.0, dd. 9 December 2019 (SAP Amendment 3) Final version 11.0, dd. 30 June 2021 (SAP Addendum)
Trial Code:	GCT1021-01

Signature Page for GCT1021-01_SAP
Study GCT1021-01 v4.0

eSignature for Approval	[redacted] Author 30-Jun-2021 10:37:40 GMT+0000
eSignature for Approval	[redacted] [redacted]Statistician 30-Jun-2021 10:39:10 GMT+0000
eSignature for Approval	[redacted] Sponsor 30-Jun-2021 11:00:37 GMT+0000

Signature Page for GCT1021-01_SAP
Study GCT1021-01 v4.0

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Statistical Analysis Plan – Amendment 3

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1. List of Abbreviations and Definition of Terms

Abbreviation	Term
ADA	Anti-drug antibody
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Curve
BMI	Body Mass Index
BP	Blood Pressure
bpm	Beats per Minute
BSL	Baseline
CA-125	Cancer Antigen 125
C_{max}	maximum Concentration
CMV	Cytomegalovirus
CNS	Central Nervous System
CR	Complete Response
CRF	Case Report Form
CRPC	Castration-Resistant Prostate Cancer
CT	Computed Tomography
CTCAE	Common Toxicity Criteria for Adverse Events
CV%	Coefficient of Variation
DDS	Dose-Determining Set
DLT	Dose Limiting Toxicity
DMC	Data Monitoring Committee
DoR	Duration of Confirmed Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
FAS	Full Analysis Set
FDA	U.S. Food and Drug Administration
GCIG	Gynaecological Cancer Intergroup
GGT	Gamma-GT
HCC	Hepatocellular Carcinoma
ICH	International Conference on Harmonization
IHC	Immunohistochemistry

[redacted]

IMP	Investigational Medicinal Product (enapotamab vedotin)
IRC	Independent Review Committee
ITT	Intention-To-Treat
LDH	Lactate Dehydrogenase
LLoQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
MMAE	Monomethyl auristatin E
MTD	Maximum Tolerated Dose
NCI	National Cancer Institute
NE	Not Evaluable
NLCB	No Longer Clinically Benefitting
NSCLC	Non-Small Cell Lung Cancer
OD	Oculus Dextrus (right eye)
ORR	Objective Response Rate
OS	Oculus Sinister (left eye)
PD	Progressive Disease
PFS	Progression-Free Survival
PK	Pharmacokinetic
PR	Partial Response
PSA	Prostate-Specific Antigen
RECIST	Response Evaluation Criteria in Solid Tumors
ROC	Receiver Operating Curve
SAE	Serious Adverse Event
SAF	Safety Set
SAP	Statistical Analysis Plan
SD	Stable Disease
SOD	Sum of Diameters
T3	Triiodothyronine
T4	Thyroxine
TNM	Tumor Nodes Metastasis
ToR	Time to Onset of Response
TSH	Thyroid Stimulating Hormone
ULN	Upper Limit of Normal ranges
WHO	World Health Organization

[redacted]

2. Introduction

This Statistical Analysis Plan is written for the clinical trial GCT1021-01 conducted in Denmark, Belgium, UK, US, the Netherlands and Spain (the last two added for the expansion part of the trial). The ICH guideline E3 "Structure and Content of Clinical Study Reports" is used as a guide to the writing of the plan.

3. Trial Design and Objectives

3.1 Trial Objectives

3.1.1 Primary Objective

- To determine the maximum tolerated dose (MTD) and to establish the safety profile of enapotamab vedotin in a mixed population of subjects with specified solid tumors.

3.1.2 Secondary Objectives

- To evaluate the safety laboratory parameters of enapotamab vedotin in a mixed population of subjects with specified solid tumors.
- To establish the pharmacokinetic (PK) profile and evaluate immunogenicity of enapotamab vedotin after single and multiple infusions.
- To evaluate the antitumor activity of enapotamab vedotin in a mixed population of subjects with specified solid tumors.
- To evaluate Axl expression in tumor biopsies from a mixed population of subjects with specified solid tumors.

3.1.3 Exploratory Objective

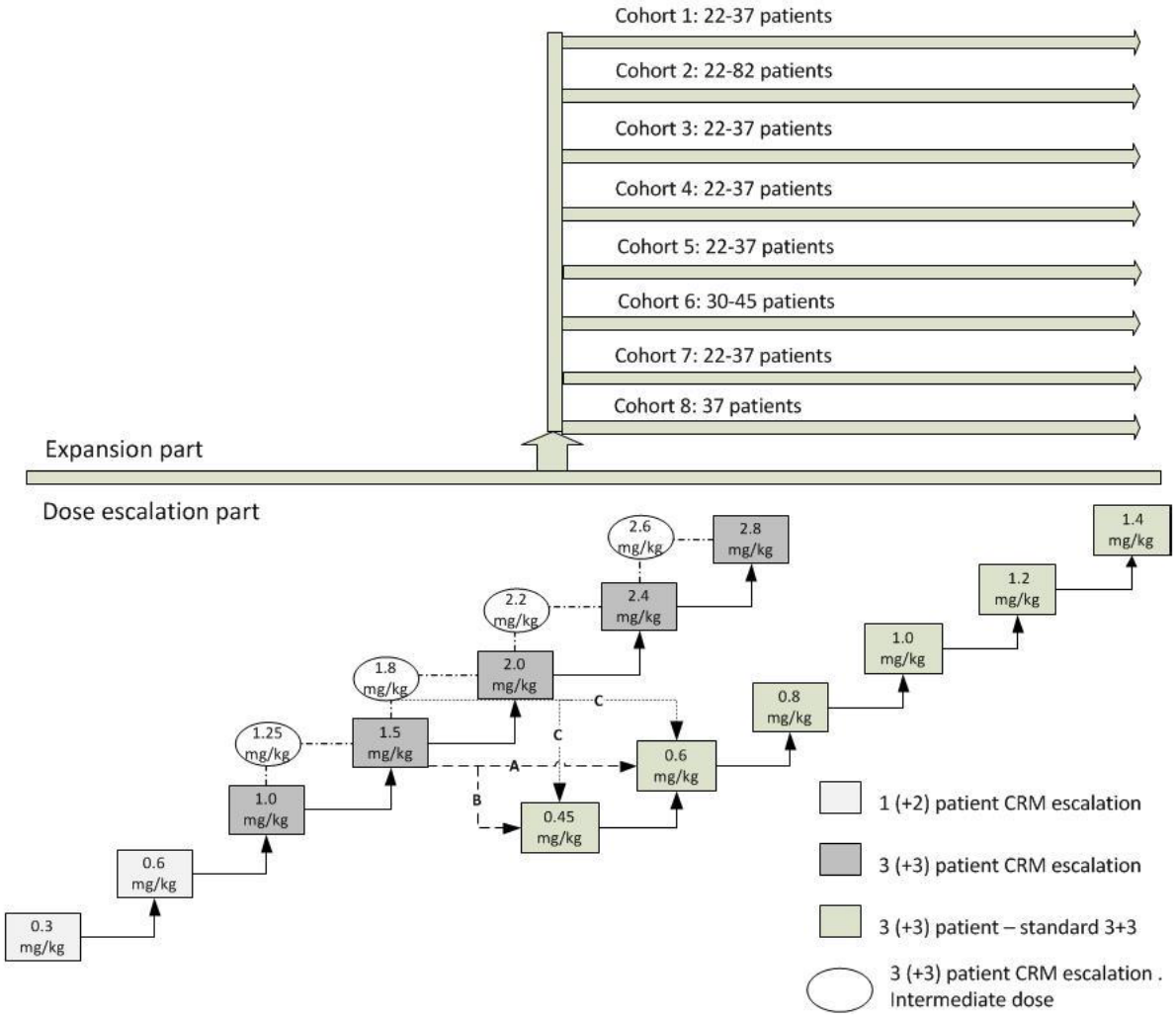
- To explore biomarkers predictive of response and resistance to enapotamab vedotin.

3.2 Trial Design

The trial design is available in section 5 Trial Design of the protocol final version 10.0, dd. 9 December 2019.

[redacted]

Figure 1. Overview of trial design



Footnote: description of A, B and C can be found in the protocol final version 10.0, dd. 9 December 2019, section 5.1.

3.3 Sample Size Justification

In the dose-escalation 1Q3W-arm, 28 subjects are expected and the maximum number of subjects is set to 41. The dose-escalation 3Q4W–arm will be including 15-36 subjects.

The expansion cohorts will include up to 349 subjects. The information obtained from the above subjects is considered adequate to provide sufficient basis for the planning and design of further trials.

In Cohorts 1, 3, 4, 5 and 7, the aim is to enroll 22 subjects per cohort. However in order to obtain evaluable fresh tumor biopsies from at least 15 subjects per cohort, up to 15 subjects may be additionally recruited per cohort leading to a maximum of 37 subjects enrolled per cohort except for Cohort 2 where up to 60 additional subjects will be enrolled in order to further understand the safety, tolerability, efficacy, and biomarker

[redacted]

findings of enapotamab vedotin as an efficacy signal has been observed in this population of non-small cell lung cancer (NSCLC) subjects without line/ALK mutations.

A sub-group of the subjects in Cohort 2 (up to 30 subjects), may be enrolled on a dose of 1.8 mg/kg to further understand the tolerability profile and to extend the therapeutic window of enapotamab vedotin.

Furthermore, if considered necessary (as assessed by the Data Monitoring Committee [DMC] and the sponsor Safety Committee [SC]) selected cohort(s) might be explored on both dosing schedules from the dose-escalation without increasing the total number of subjects to be included in the trial.

In Cohort 6, 30 subjects with solid tumors (except for NSCLC, melanoma, sarcoma and ovarian cancer subjects, unless having a known AXL gene amplification) who have failed a PD-1/PD-L1 inhibitor and are able to provide the required fresh tumor biopsy are planned to be enrolled.

For further exploration of the safety and efficacy profile of the 3Q4W schedule, subjects in Cohort 6 will be enrolled on a dose of 1.0 mg/kg administered 3Q4W, which was determined to be the MTD for this schedule in the dose-escalation part of the trial. Preferably, no more than 8 subjects should be recruited for one tumor type in this cohort.

In order to obtain sufficient evaluable fresh tumor biopsies, up to 15 additional subjects may be recruited in Cohort 6 to ensure that 25 fresh biopsies are acquired. A maximum of 45 subjects may therefore be enrolled in Cohort 6. A higher number of biopsies are required in this cohort due to the mixture of tumor types being enrolled.

Cohort 8 will further explore the safety and efficacy of the 1.0 mg/kg 3Q4W schedule in NSCLC subjects without EGFR/ALK mutations. This is the same subject population as Cohort 2 where a preliminary efficacy signal was observed for the 1Q3W schedule. Cohort 8 will include up to 37 subjects with the aim to collect evaluable fresh tumor biopsies from 15 subjects. Recruitment is not linked to the number of biopsies collected and may continue up to a maximum of 37 subjects even if 15 fresh tumor biopsies have already been obtained. The benefit/risk balance will be evaluated on an ongoing basis in this cohort.

More details can be found in section 10.9 Sample Size Estimation of the protocol final version 10.0, dd. 9 December 2019.

4. General Analysis Definitions

Data will be analyzed using SAS (Version 9.4 or higher). For graphs R (Version 3.3.2 or higher) can be used in addition.

Descriptive statistics will be tabulated as follows:

- Categorical data will be summarized in contingency tables presenting frequencies and percentages.
- Continuous data will be summarized using number of non-missing values (n), mean, standard deviation, median, 25th and 75th percentiles, minimum and maximum values.
- Time to event parameters will be described using Kaplan-Meier estimates: median time, first and third quartiles along with approximate 95% confidence intervals (the default conftype=loglog in proc lifetest will be used). The 3, 6, 9 and 12 months event-free rates will also be presented together with the 95% confidence intervals.

[redacted]

The results will be presented by 1Q3W and 3Q4W dose-escalation and expansion parts separately. Results will be presented for both trial parts unless specified otherwise.

The results will be presented by groups and total. In the dose-escalation 1Q3W and 3Q4W arms of the trial, groups are defined by dose levels. In the expansion part, groups are defined by cohort, dose level and dosing regimen.

For the dose-escalation part, all seven dose levels from the 1Q3W regimen together with a 'total' will be presented on one page. And similar for the 3Q4W regimen in the dose-escalation part, all four dose levels will be presented together on one page including a 'total'.

For the expansion part the following grouping should be done: Cohorts 1, 3, 4, 5, 6 and 7 on one page and cohort 2 with 2.2 mg/kg, cohort 2 with 1.8 mg/kg, cohort 2 total, cohort 8, total across 1Q3W and total across 3Q4W on one page.

All data will be listed by trial part, cohort for expansion part, dose schedule, dose level, subject number and visit (if applicable).

In general, in plots where subject data are grouped together (e.g. plots of means), the ticks on the time-axis will denote the nominal visit numbers (e.g. Scr, C1D1, C1D2 , C1D4 etc.) separated with distances proportionate to the difference between the time-points of the corresponding visits in the relevant dose schedule (cf. the Visit Number and Day/Week rows of table of assessments in section 8 of the protocol final version 10.0, dd. 9 December 2019). Unscheduled visit data will not be included. In plots where individual subject data are plotted vs. time, the time on the horizontal axis will denote the actual time since C1D1. Unscheduled visit data will be included in these plots.

In tables and listings presenting data by visit, the visit names (Screening, Cycle 1 Day 1, Cycle 1 Day 2, …, End of Treatment, Safety Follow-up, Subject Follow-up and End of Trial) will be used or their abbreviated term (Scr, C1D1, C1D2, …, EOTrt, Saf FU, Pat FU, EOTrial).

In tables and listings presenting coded data (medical history, prior and concomitant medications, adverse events, prior and subsequent cancer therapies), the dictionary and the version used will be mentioned in the footnote.

When data until a certain date needs to be included in the analysis, the cut-off date will be defined as this date. If no cut-off needs to be applied, the cut-off date will be defined as the date of data extraction.

4.1 Trial Period and Visit Window Definitions

4.1.1 Trial Periods

Screening period will be defined as the period before the date of first investigational medicinal product (IMP) administration (enapotamab vedotin).

Treatment period including safety follow-up period will be defined as the period between the date of first IMP administration and the date of last IMP administration + 30 days or the end of treatment visit whichever comes later.

Follow-up period will be defined as the period between the end of treatment period including safety follow-up period + 1 day and the date of last contact.

[redacted]

4.1.2 Visit Windows

Visit windows are defined in the protocol. Those will not be used in the analysis to avoid excluding important data due to dates outside visit windows. Tables by visit will assume that observations are from the recorded visit irrespective of the date specified.

4.2 Planned Analyses

The final analysis of trial data will be performed when the trial is completed after the end of the expansion part and will be based on all subject data of the dose-escalation and expansion parts.

This analysis will be based on locked databases with clean data. A full integrated clinical trial report will be produced when the trial is completed.

An interim analysis for futility will be performed after 22 subjects per cohort if there are <15 subjects with evaluable fresh biopsies in the corresponding cohort. In cohorts 1-5: if there are ≤ 2 responders in the first 22 subjects, further recruitment to the corresponding cohort may be stopped. In cohort 7 the futility threshold is ≤ 3 responders in the first 22 subjects. While the focus in this analysis will be on objective response, other data including baseline characteristics, biologic activity (reduction in tumor size, CA 125 and PSA), safety, tolerability and PK as presented in the DMC packages will also be reviewed. Any decision will also consider supporting information from the other cohorts.

Subjects should be treated and able to reach the cycle 2 day 15 visit for 1Q3W schedule and cycle 2 day 22 for 3Q4W schedule (at least one post-baseline CT scan or discontinued before) in order to be included in the interim analyses for futility.

In Cohorts 6 and 8, the safety and anti-tumor activity will be evaluated on an ongoing basis during the trial.

As part of preparations for subsequent trials, further exploratory analyses of subsets of data may be performed.

4.3 Definition of Populations (Analysis Sets)

Screening failures and subjects who were screened but never started treatment will be listed and summarized as described below, but will not be included in any of the analyses and summary tables based on Full Analysis Set, Safety Set or Dose-Determining Set below.

4.3.1 Full Analysis Set

The Full Analysis Set (FAS) consists of all subjects who have been exposed to enapotamab vedotin (i.e. at least one dose of IMP). Subjects will be classified according to the assigned treatment/dose (planned dose level and schedule).

4.3.2 Safety Set

The Safety Set (SAF) consists of all subjects who receive at least one dose of enapotamab vedotin. Subjects will be classified according to actual treatment received (dose level based on the first enapotamab vedotin administration).

4.3.3 PK Analysis Set

The PK Analysis Set consists of all subjects who have been exposed to enapotamab vedotin (i.e. at least one dose of IMP) and who have at least 1 post-dose PK measurement.

[redacted]

4.3.4 Dose-Determining Set (Dose-Escalation Part only)

The Dose-Determining Set (DDS) consists of all subjects from the safety set who either meet the minimum exposure criterion and have completed the DLT observation period, or have experienced a DLT during cycle 1. This constitutes an evaluable subject for the determination of MTD.

A subject is considered to have met the minimum exposure criterion at a dose level if enapotamab vedotin has been administered for at least 90% of the planned dose in each of the infusions.

DLT observation period: subjects who do not experience a DLT during the first cycle are considered to have sufficient safety evaluations if they have been observed for a minimum length following the first dose defined in Table 2 below, and are considered by both the Sponsor and the DMC to have enough safety data to conclude that a DLT did not occur.

Table 2. Minimum exposure for inclusion in DDS set.

Trial part	Number of infusions	Number of observation days in Cycle 1
Dose-escalation 1Q3W	1	21
Dose-escalation 3Q4W	3	28

Details of the analysis sets will be included in the "Classifications of Analysis Populations" plan. The applicable analysis set will be stated in the outputs.

4.4 Subgroup Definitions

Subgroup analyses for the following factors are planned for the expansion part:

- Cancer type - only for cohort 6
- Cohort 2: up to 2 treatment lines of prior therapy versus more than 2 treatment lines of prior therapy within the 2.2 mg/kg dose level - only for cohorts 2 and 8
- Age (age<65 years and age ≥65 years) - only for cohorts 2 and 8
- Gender - only for cohorts 2 and 8
- Histology: squamous versus non-squamous - only for cohorts 2 and 8
- ECOG performance score at baseline (0 vs 1)
- Smoking status (current smoker, past smoker, non-smoker)
- Amendment 6 period (inclusion before amendment 6, after amendment 6)
- Best response to latest regimen (CR, PR, SD, PD)
- Histology results (Chondrosarcoma vs other) – Cohort 5

Other sub-group analyses including biomarkers may be performed. Due to the low expected number of subjects per site no investigation of site effects are planned.

Subgroup analysis will only be made if there is a sufficient split in subjects (>=5 subjects).

The following outputs will be repeated for each of the subgroups mentioned above:

- Forest plot for confirmed objective response rate,
- PFS (KM estimates and plots)

[redacted]

- OS (KM estimates and plots)

4.5 Treatment Assignment and Treatment Arms

4.5.1 Dose-Escalation Part

- 1Q3W schedule: Enapotamab vedotin, 7 main dose levels: 0.3, 0.6, 1.0, 1.5, 2.0, 2.4 and 2.8 mg/kg, and 4 optional intermediate dose levels 1.25, 1.8, 2.2 and 2.6 mg/kg. Further escalation with steps of 0.4 mg/kg and de-escalation by 0.2 mg/kg is allowed, if the MTD has not been declared at a dose level up to 2.8 mg/kg.
- 3Q4W schedule: Enapotamab vedotin, main dose levels: 0.6, 0.8, 1.0, 1.2 and 1.4 mg/kg. If the 1.4 mg/kg is reached without significant safety concerns and it is considered safe to escalate above 1.4 mg/kg, the escalation may continue to higher dose levels with increments up to 20% using the standard 3+3 rules. The starting dose is expected to be 0.6 mg/kg (a dose level of 0.45 mg/kg may be added).

4.5.2 Expansion Part

- Enapotamab vedotin: schedule and dose from the dose-escalation part recommended by the DMC and confirmed by the sponsor safety committee based on benefit-risk assessment.
    - Cohort 1: NSCLC subjects with classical sensitizing EGFR mutations and/or EGFR mutations targeted by third generation TKIs - 1Q3W schedule, 2.2 mg/kg
    - Cohort 2: NSCLC subjects without activating EGFR mutations or ALK rearrangements - 1Q3W schedule, 1.8 mg/kg or 2.2 mg/kg
    - Cohort 3: Melanoma subjects with BRAF V600 mutation - 1Q3W schedule, 2.2 mg/kg
    - Cohort 4: Melanoma subjects with BRAF V600 wild-type - 1Q3W schedule, 2.2 mg/kg
    - Cohort 5: Sarcoma subjects - 1Q3W schedule, 2.2 mg/kg
    - Cohort 6: Subjects with solid tumors, excluding NSCLC, melanoma, ovarian cancer and sarcoma subjects unless having a known AXL gene amplification (preferably no more than 8 subjects should be recruited for one tumor type) - 3Q4W schedule, 1.0 mg/kg
    - Cohort 7: Platinum-resistant ovarian cancer subjects - 1Q3W schedule, 2.2 mg/kg
    - Cohort 8: NSCLC subjects without activating EGFR mutations or ALK rearrangements - 3Q4W schedule, 1.0 mg/kg

4.6 Calculated Variables

The following general definitions will be used throughout the trial:

- Baseline is defined as the latest recorded measurement made before the first IMP administration (trial day 1). Measurements done on the same date as the first IMP administration will be considered as done before the first IMP administration unless specified otherwise. For PK variables, the first IMP administration will be time 0.

[redacted]

- Change from baseline is defined as the post-baseline value – baseline value. Change from baseline will be missing when either post-baseline or baseline value is missing.
- Percent change from baseline is defined as 100*(post-baseline value – baseline value)/baseline value. If the baseline value is 0 and the post-baseline value is 0, the change from baseline and the percent change from baseline are both 0. If the baseline value is 0 and the post-baseline value is not 0, the change from baseline is the same as the post-baseline value and the percent change from baseline will be undefined (missing).

The following variables will also be computed for the analyses described later on:

- Time (in months) from initial diagnosis of primary site to start date of IMP: (date of first IMP administration – date of first diagnosis)/30.4375.
- Time (in months) since most recent recurrence/relapse or progression to start date of IMP: (date of first IMP administration – date of most recent recurrence/relapse or progression)/30.4375.
- Time (in months) since (last) biopsy to start date of IMP: (date of first IMP administration – date of (most recent) biopsy before or on the start date of IMP)/30.4375. Time since biopsy will be included in the listing, time since last biopsy will be included in the biopsy table (only one result per subject).
- Time (in months) since biopsy to start date of IMP for post-baseline biopsy data: (date of (most recent) biopsy - date of first IMP administration +1)/30.4375.
- Time (in months) since most recent recurrence/relapse or progression to date of most recent biopsy: (date of most recent biopsy – date of most recent recurrence/relapse or progression)/30.4375.
- Time (in months) between fresh biopsy and archival biopsy (when both are available): (date of fresh biopsy – date of archival biopsy)/30.4375 (only listed).
- Duration of exposure (days): (end date of IMP – date of first IMP administration + 1),
    - with end date of IMP defined as min (date of last IMP administration + 20 days, last contact date, date of death, cut-off date) – *For 1Q3W schedule*
    - with end date of IMP defined as min (date of last IMP administration + 27 days (if D1 of cycle) or 20 days (if D8 of cycle) or 13 days (if D15 of cycle), last contact date, date of death, cut-off date) – *For 3Q4W schedule*
- Actual cumulative dose (mg): sum of all actual doses administered.
- Planned cumulative dose (mg) – only used for calculation of relative dose intensity: Allocated dose level * weight in kg * number of cycles initiated for 1Q3W and allocated dose level * weight in kg * 3 * number of cycles initiated for 3Q4W. For subjects whose body mass index (BMI) is greater than 30 kg/m2, the formula should use a weight that, based on the subject's height, corresponds to a maximum BMI of 30. When a cycle is missed/skipped, this cycle is also included to count the number of cycles initiated.
- Dose intensity (mg/cycle): actual cumulative dose in mg divided by the number of cycles initiated.
- Relative dose intensity (%): 100 * ratio of actual cumulative dose and planned cumulative dose.
- Number of days in trial: max (last contact date, date of death) – date of first IMP administration + 1.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

4.7 Partial/Missing Dates

Partial or missing dates in general will not be imputed (medical history, previous cancer treatment).

For the calculation of the time (in months) from initial diagnosis of primary site to date of first IMP administration and time (in months) since most recent recurrence/relapse or progression to date of first IMP administration, the following imputation rules will be applied when the date of first diagnosis or date of most recent recurrence/relapse or progression is incomplete:

- If the day is missing: first day of the month
- If the day and month are missing: first day of July.
- If the day and month are missing and if the year is the same as the year of first IMP administration: leave missing.

For the assignment to prior or concomitant medication the following rules will be applied in case of incomplete or missing dates:

- If medication is ongoing or end date is missing then medication will be considered as concomitant and missing date(s) will not be imputed.
- If end date is incomplete: if the day is missing: the end date will be imputed with the last day of the month; if the day and month are missing: the end date will be imputed with min(31 December of the year, last contact date, date of death).

The imputed dates will only be used for the assignment to prior or concomitant and will not be used in any other calculation and will not be listed.

For new anti-cancer therapy, when the start date is partial or missing, the date will be imputed:

[redacted]

- If start date is missing, but end date is not missing: the start date will be set to the end date.
- If start date remains missing, the start date will be set to the minimum of (last contact date and date of death).
- If start date is incomplete: if the day is missing: the start date will be imputed with the last day of the month; if the day and month are missing: the start date will be imputed with min (31 December of the year, the last contact date, date of death, end date if not missing).

The imputed dates will only be used to define the start of the new anti-cancer therapy for progression free survival and will not be used in any other calculation and will not be listed.

For the assignment of adverse events (AE) the following rules will be applied in case of missing or incomplete start date:

- If end date is before the date of first IMP administration, the adverse event will be assigned to the pre-treatment period (reported with medical history) and the start date will remain missing/incomplete;
- If start date is missing and end date is after or on the date of first IMP administration or the end date is missing, the start date will be imputed by the date of first IMP administration ;
- If start date is incomplete and end date is after or on the date of first IMP administration or the end date is missing, the start date will be imputed as follows:
    - If the day is missing and if the start date and date of first IMP administration share the same month and year, the missing start day will be imputed as the day of first IMP administration. If the start date month is after the month of first IMP administration, day will be imputed as the first (i.e. 01-MMM-YY);
    - If the day and month are missing and if the start date and date of first IMP administration share the same year, day and month will be imputed as the day and month of first IMP administration. If the start date year is after the year of first IMP administration, the month and day will be imputed as January first (i.e. 01-JAN-YY).

The imputed date will only be used for the assignment of the treatment-emergent adverse event flag/trial periods and will not be used in any other calculation (unless specified otherwise) and will not be listed.

4.8 Methods to Be Used For Handling Missing Data

All available data will be included in data listings and tabulations. Imputed dates will not be included in the listings.

No imputation of missing data is planned for safety endpoints and PK endpoints. If outliers are detected, a robustness analysis where the outlier effect is reduced or eliminated may be considered.

Missing data for tumor response related variables will be handled/imputed in accordance with the RECIST criteria version 1.1[2] and for subjects with ovarian cancer according to RECIST 1.1 in combination with CA-125 as defined by the Gynecological Cancer Intergroup[3].

[redacted]

For the expansion part, imputation methods might be introduced in case of incomplete tumor assessments for the analysis of the sum of diameters (SOD) and documented in a SAP amendment.

4.9 Changes to Protocol

Changes compared to protocol final version 10.0, dd. 9 December 2019:

Table 4 Evaluation of Response in section 15.1 of this SAP has been updated by clarifying the definition of not-evaluable (NE).

Subgroup analysis for Cohort 2 (up to 2 lines of prior therapy versus more than 2 lines of prior therapy within the 2.2 mg/kg dose level), Age (age<65 years and age ≥65 years), Gender, Histology: squamous versus non-squamous, ECOG performance score (0 versus 1), smoking status ((current smoker, past smoker, non-smoker), amendment 6 period (inclusion before amendment 6, after amendment 6), best response to latest regimen (CR, PR, SD, PD) and histology results (Chondrosarcoma vs other) – Cohort 5 are added.

IRC tumor assessments are not presented, the BOR and CBOR based on IRC are listed only.

PSA results (when available) and urinalysis results will only be listed.

The Safety Set is updated by removing the condition to have a valid post-baseline safety assessment as it is considered appropriate to keep all exposed subjects in the safety set to align with ICH guidelines.

Additional adverse events tables are added for completeness.

One additional analysis set is added: PK analysis set.

The interim analysis at the end of the dose-escalation part is removed as data from the dose-escalation and expansion part will be presented together as described in section 4.2.

5. Trial Subjects

5.1 Disposition of Subjects

Screening failures including failure reason and re-screening information will be presented in a listing. Subjects screened but never started trial treatment will be included in the same listing. The number of screen failure and the screen failure reasons will be tabulated.

The number of subjects in each analysis set as defined in section 4.3 will be tabulated. The reason(s) for subjects not included in each population will be presented in a listing.

The frequency of subjects treated, of subjects who discontinued the trial treatment and of subjects who terminated the trial will be given for the full analysis set (FAS). The primary reason for discontinuation of the trial treatment and terminating the trial will be summarized. The details of the 'other reason' will be included in the listing.

Subject dispositions will also be presented in flow diagrams in accordance with the current CONSORT statement[1].

5.2 Protocol Deviations

The important major protocol deviations will be summarized. The details will be listed.

In addition, Covid-19 related PDs will be listed separately:

- All important PDs related to Covid-19;

[redacted]

- All non-important PDs related to Covid-19 (this will be major, non-important as well as minor, non-important);
- Subject listing of missed/changed visits;
- Subject listing of assessments missed due to visits impacted by Covid-19.

A summary table of the above might be added to evaluate the impact of Covid-19.

Protocol deviations will be defined in the protocol deviations plan.

5.3 In- and Exclusion Criteria

Listing of all in- and exclusion criteria not met as completed on the "Inclusion/Exclusion criteria not met" page of the eCRF will be provided.

Information of informed consent [redacted] will be presented in the disposition listing.

6. Demographic Characteristics

Descriptive statistics with respect to subject characteristics at baseline will be displayed for the FAS.

The variables to be summarized are:

- Gender (Male/Female)
- Age (years, continuous and categorical: age<65 years and age ≥65 years)
- Race (White, Black or African American, Native Hawaiian or other Pacific Islander, Asian, American Indian or Alaska native, Other)
- Ethnic origins (Hispanic or Latino, Not Hispanic or Latino)
- Region (US, Europe)
- Weight (kg)
- Height (cm)
- BMI (kg/m²)
- HbA1c
- Smoking history
    - Usage (Current smoker, Past smoker, Non-smoker)
- Drinking history
    - Usage (Daily, 3-6 times per week, 1-2 times per week, Less than 4 times per month, None)
- Contraception data
    - Subject considered as sterilized or infertile (Yes, No)
    - Reason (Surgical sterilization, Postmenopausal, Other)
- Contraception details (listed only)
    - Subject practice adequate contraception (Yes, No)

[redacted]

- Type of contraception (Pills, Implant, Vaginal device, Injections, Transdermal patches, Other)

Details of the other categories mentioned above will be added to the listings.

7. Baseline Disease Characteristics

Descriptive statistics with respect to subject disease characteristics at baseline will be displayed for the FAS.

The variables to be summarized are:

- ECOG performance score (0-5). Note: at entry only subjects with an ECOG performance score of 0 and 1 are allowed)
- Cohort 2: up to 2 treatment lines of prior therapy versus more than 2 treatment lines of prior therapy within 2.2 mg/kg group
- Lactate dehydrogenase (LDH) for melanoma subjects only
- % Axl-positive tumor cells (%>=1+) – Expansion part only
- Type of cancer at initial diagnosis (NSCLC, Follicular or Hürthle cell thyroid cancer, Papillary thyroid cancer, Medullary thyroid cancer, Anaplastic thyroid cancer, Ovarian cancer, Cervical cancer, Endometrial cancer, Melanoma, and other primary sites as per enrolment in the expansion part)
- Tumor stage at initial diagnosis (I, IA, IB, II, IIA, IIB, III, IIIA, IIIB, IV, IVA, IVB, IVC) by indication.
- Tumor stage at screening (I, IA, IB, II, IIA, IIB, III, IIIA, IIIB, IV, IVA, IVB, IVC) by indication.
- Histological results (see CRF for the details) by indication
- Histological subtype (see CRF for the details) by indication
- Mutational status (EGFR mut, ALK rearrangement, BRAF, NRAS, None) and mutational sub-term (T790M, L858R, …) combined
- Time (in years) from initial diagnosis to start date of IMP administration (continuous and in classes: <1 year, 1-<2 years, 2-<3 years, 3-<4 years, 4-<5 years, >=5 years)
- Snellen score (OD and OS)
- Number of metastatic sites per subjects (1, 2, 3, 4, >=5)
- Number of subjects with CNS metastases
- Number of subjects with liver metastases
- Sum of reference diameters of target lesions (mm)
- CA-125 as continuous and as categorical: <=ULN, >ULN (for Ovarian cancer subjects only)
- Tumor classification (TNM) at screening and initial diagnosis and histological grade will be listed only

[redacted]

8. Biopsy Information

Descriptive statistics with respect to the biopsy information at baseline will be displayed for the FAS.

The variables to be summarized are:

- Biopsy performed (Yes, No) at screening*
- Type of biopsy (Fresh, Archived) at screening*
- Location of biopsy (multiple answers possible when different biopsies were done at screening)
- Time since last biopsy before start of IMP to start date of IMP (months)
- Time since biopsy to start date of IMP (months) will be added in the listing for each biopsy performed (before or after the start date of IMP)
- Number of subjects with evaluable biopsies before first IMP administration and after (by visit)
- Reason for biopsy failure (by visit) , listed only (free text)

* independent if at screening or re-screening visit.

Details of the other categories mentioned above will be added to the listings.

9. Medical and Surgical History

Medical conditions and surgeries will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

The medical conditions (separately for active (ongoing) and non-active conditions) and the surgeries will be tabulated separately, by system organ class (SOC) and preferred term (PT) for the FAS. Tables will be ordered by decreasing frequency of SOC and by decreasing frequency of PT within SOC. As mentioned in the section 17.2 of Adverse Events, the adverse events collected during the pre-treatment period will be tabulated together with the medical history.

All details will be listed.

10. Prior Cancer Therapies

Prior systemic cancer therapies will be summarized for the FAS as described below.

Prior systemic therapies in the metastatic setting will be listed and tabulated by first and fourth Anatomical Therapeutic Chemical class (WHO-DD dictionary, ATC 1 name and ATC 4 name) for the FAS. ATC classes will be ordered by decreasing frequency. In addition, the latest treatment line, the latest treatment line -1, the latest treatment line -2, and the latest treatment lines – (>=3) of prior cancer therapies will be tabulated in the same way to see what the subjects received just before entering the trial and earlier to see the influence on Axl expression.

Prior radiation therapies and prior surgeries will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and presented separately by system organ class and preferred term (ordered by decreasing frequency of SOC and by decreasing frequency of PT within SOC).

In addition, the number of prior treatment lines (not taking into account surgeries and radiation, restricted to systemic therapies in the metastatic setting) will be summarized by means of descriptive statistics and by category (1, 2 and ≥3) and the best response to

[redacted]

the latest treatment line, the latest treatment line -1, the latest treatment line -2, and the latest treatment lines – (>=3) of prior cancer therapy will be tabulated together with prior surgery related to cancer (Yes/No) and prior radiotherapy (Yes/No).

All details recorded in the eCRF will be listed.

11. Subsequent Cancer Therapies

Subsequent cancer therapies will be summarized for the FAS as described below.

Subsequent systemic cancer therapies in the metastatic setting will be listed and tabulated by first and fourth Anatomical Therapeutic Chemical class (WHO-DD dictionary, ATC 1 name and ATC 4 name) for the FAS. ATC classes will be ordered by decreasing frequency.

On-study radiation therapies and surgeries will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and presented by system organ class and preferred term. SOC and PT (within SOC) will be ordered by decreasing frequency.

All details will be listed.

12. Procedures

Non-protocol medical procedures will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

The medical procedures will be tabulated by system organ class (SOC) and preferred term (PT) for the FAS. Table will be ordered by decreasing frequency of SOC and by decreasing frequency of PT within SOC.

All procedures will be listed.

13. Prior and Concomitant Medications

Prior and Concomitant medications will be classified according to World Health Organization Drug Dictionary.

Medications will be reported according to the following two distinct categories:

- Prior when they start and end before the first day of trial treatment.
- Concomitant when they start before the first day of trial treatment and stop or continue after the first day of trial treatment, or when they start on or after first day of trial treatment.

The number and percentage of subjects receiving a concomitant medication will be displayed by first and fourth Anatomical Therapeutic Chemical class (WHO-DD dictionary, ATC 1 name and ATC 4 name) for the FAS. ATC classes will be ordered by decreasing frequency.

In addition, the concomitant medications for blood transfusions will be presented separately in the same way.

Prior medications will only be listed.

All medications recorded on the (prior and) concomitant medications eCRF page, classified as either prior or concomitant medication, will be listed separately. The listings will include details such as indication, dose, route, frequency, and start and stop dates. Also the specific AE or medical history event will be included where applicable.

[redacted]

14. Primary Endpoint

Dose-escalation part

DLT analyses will be done on the dose-determining set (DDS) in the dose-escalation part of the trial.
The number of subjects with a DLT will be presented for each dose level and treatment schedule. In addition, a plot of the dose level by subject (in order of inclusion) will be presented marking the DLTs observed (see CRM examples in the protocol final version 10.0, dd. 9 December 2019, Appendix II) and also indicating the subjects which are not evaluable for DLT (not part of the DDS) for each treatment schedule.

Dose-escalation and Expansion part

The safety profile of enapotamab vedotin will be established based on the safety outputs mentioned in section 0.

15. Efficacy Evaluation

Efficacy results will be presented on the FAS unless specified otherwise.

15.1 Response

The response results from the dose-escalation part and the expansion part will be presented using summary statistics.

Response will be defined according to RECIST 1.1. For subjects with ovarian cancer (Cohort 7) the response will be defined on the combination of the response according to RECIST 1.1 and CA-125 (see below in section 15.1.2).

15.1.1 Response according to RECIST 1.1

Response in solid tumor cancers will be assessed in accordance with the RECIST criteria version 1.1[2].

Table 4. Evaluation of Response

Target Lesions	Non-target Lesions	New Lesions	Response
CR	CR	No	CR
CR	Non-CR/Non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-PD or not all evaluated	No	PR
SD	Non-PD or not all evaluated	No	SD
Not all evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD

[redacted]

Any	PD	Yes or No	PD
Any	Any	Yes	PD

Confirmation:

PR and CR: changes in tumor measurements that are confirmed* by repeat assessments performed no less than four weeks after the criteria for response are first met are called confirmed responses. Onset of PR or CR without such confirmation is called unconfirmed.

SD: follow-up measurements must have met the SD criteria at least once and for a minimum time period of 6 weeks (± 7 days) after first treatment.

In the dose-escalation, response evaluation will be performed by the investigator. In the expansion, response evaluation will be performed by the investigator as well as a group of external medical experts, the independent review committee (IRC). Each subject will be assigned one of the following categories for each assessment:

1) CR,
2) PR,
3) SD,
4) PD, or
5) Not Evaluable (NE)

The best overall response is the best response recorded from the start of the treatment until disease progression/recurrence.

A subject is defined as an objective responder if he/she has a best overall response assessment of CR or PR.

Subjects in response categories 3, 4 and 5 (SD, PD or NE) are considered as non-responders.

Subjects with a best overall response assessment of CR, PR or SD are considered to be in disease control.

Confirmed* responses and all responses (including confirmed and unconfirmed responses) will be presented separately for the objective response (yes/no) and disease control (yes/no) parameters.

[* The following sequences (assessments over time) will be counted as confirmed response:

- CR-CR = CR confirmed
- PR-PR = PR confirmed
- PR-CR = PR confirmed

Note: the sequence CR-PR is not allowed and should be queried. The PR should be corrected to PD because of reappearance of disease. Imaging charter must make sure that prior scan is corrected to PR if believed when seeing the following scan to be only PR. This way CR-PR should not occur if the reader interprets this as a PR confirmed. Otherwise it would be CR-PD which would qualify as confirmed SD for the confirmed visit response if minimum duration criteria for SD is met.

[redacted]

Intermediate missing (NE) scan evaluations between the response scan and the confirmation scan are allowed, e.g. the sequences PR-NE-PR and PR-NE-NE-PR will be considered PR confirmed.

In all cases the scan that confirms the first scan with CR/PR must occur no sooner than 4 weeks after the first scan.

A subject with sequences that qualify both as PR confirmed and CR confirmed, e.g. PR-PR-CR-CR would be considered a CR confirmed. Note that the date of confirmed response will be the date of the first PR.

If PR or CR are not confirmed, the PR or CR response will be SD when the scan is on or after 35 days and NE when the scan is before 35 days. The 35 days takes into account the minimal 6-weeks duration +/- 1 week window.]

A forest plot including the subgroups defined for cohorts 2 and 8 and for cohort 6 as mentioned in section 4.4 will be presented for investigator.

BOR and CBOR based on IRC data will be listed only. All other IRC results will not be included in the analysis. They will be kept in the derived datasets.

15.1.2 Response according to CA-125

Subjects with ovarian cancer will also be evaluated according to CA-125.

A CA-125 response (PR) is defined as at least a 50% reduction in CA-125 levels from a pretreatment sample. The response must be confirmed and maintained for at least 28 days. Subjects can be evaluated according to CA-125 only if they have a pretreatment sample that is at least twice the upper limit of the reference range and within 2 weeks before starting the treatment.

More information on the rules that apply to the CA-125 data is available in section 10.4 of the protocol final version 10.0, dd. 9 December 2019.

The date when the CA-125 level is first reduced by 50% is the date of the CA-125 response.

To calculate response, an analysis should be used that includes all subjects with an initial CA-125 level of at least twice the upper limit of the reference range as eligible and evaluable.

In addition, as a separate analysis, those subjects who have a CA-125 response and whose CA-125 level falls to within the reference range can be classified as CA-125 complete responders. Subjects who have a fall of CA-125 to within the reference range but whose initial CA-125 was less than twice the upper limit of the reference range have not had a CA-125 response and cannot therefore be classified as a CA-125 complete responder.

The best overall response for both parameters (CA-125 response and CA-125 complete response) will be presented.

15.1.3 Response according to RECIST 1.1 and CA-125 combined (Ovarian cancer only) – Expansion Part

For subjects with ovarian cancer in the expansion part, responses will also be evaluated and reported according to RECIST 1.1 in combination with CA-125 as defined by the Gynecological Cancer Intergroup[3] (see table 5).

[redacted]

Table 5. Best Overall Response in Subjects with Initial Measurable Disease and Evaluable by CA-125, combining both criteria

Target Lesion~	Non Target #	New Lesion	CA-125	Overall Best Response	Best RECIST 1.1 response for CR and PR also requires it to be confirmed and maintained for at least 28 days if response is primary end point
CR	CR	No	Normal	CR	
CR	Non-CR Non-PD	No	Not PD	PR	
CR	CR	No	PR but not normal	PR	
CR	NE	No	PR	PR	
PR	Non-PD or NAE	No	Not PD	PR	
NAE	Non-PD	No	PR	PR	
PD or New >28 days from CA-125 PR *			PR	PR	
SD§	Non-PD	No	PR	PR	
SD§	Non-PD or NAE	No	Not PR and not PD	SD	
PD or New ≤ 28 days from CA-125 PR*			PR	PD	
PD	Any	Yes or No	Any	PD	
Any	PD	Yes or No	Any	PD	
Any	Any	Yes	Any	PD	
Any	Any	Yes or No	PD	PD	

~ target lesions include up to 5 measurable lesions (2 per organ) as defined by RECIST 1.1.
# non-target lesions include ascites and peritoneal thickening which are not measurable according to RECIST 1.1.
* subjects who have a CA 125 response that occurs more than 28 days from PD according to RECIST 1.1 are considered a PR, according to best response, but PD if the RECIST 1.1 PD is within 28 days of CA 125 response.
§ the minimum time interval between 2 measurements for classification as stable disease is 6 weeks (± 7 days).
NE, Not evaluated; NAE, not all evaluated.

Source: Definitions for Response and progression of ovarian cancer incorporating RECIST 1.1 and CA-125 agreed by the Gynaecological Cancer Intergroup (GCIG) – Rustin et All[3]

[redacted]

Best overall responses by investigator will be tabulated as in the example of the guideline[3].

Progression or Recurrence based on serum CA 125 levels (PD in the table above) will be defined on the basis of a progressive serial elevation of serum CA 125, according to the following criteria:

A. Subjects with elevated CA-125 pretreatment and normalization of CA-125 must show evidence of CA-125 greater than, or equal to, two times the upper normal limit on two occasions at least one week apart or

B. Subjects with elevated CA-125 pretreatment, which never normalizes must show evidence of CA-125 greater than, or equal to, two times the nadir value on two occasions at least one week apart or

C. Subjects with CA-125 in the normal range pretreatment must show evidence of CA-125 greater than, or equal to, two times the upper normal limit on two occasions at least one week apart.

In the listing of CA-125 a flag to indicate if the CA-125 fulfills the response ("PR"), "PD" or "Not PR or PD" –criteria will be added.

15.1.4 Progression-Free Survival according to RECIST 1.1

PFS is defined as the number of days from the date of first IMP administration to first PD or death whichever occurs first.

PFS will be derived for all subjects and presented graphically as well as summarized using survival analysis methods:

- Kaplan-Meier curves
- Kaplan-Meier curves by subgroups defined for cohorts 2 and 8 and for cohort 6 as mentioned in section 4.4
- Kaplan-Meier estimates.
- Kaplan-Meier estimates by subgroups defined for cohorts 2 and 8 and for cohort 6 as mentioned in section 4.4.

PFS will be censored in accordance with Table A in Appendix 3 in the FDA Guidance for Industry "Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (2007)".In summary, PFS will be censored if no event (progression or death) is observed before the first of (i) the analysis cut-off date, and (ii) the date when a new anti-cancer therapy is started. The censoring date will be the date of the last adequate tumor assessment prior to cut-off/start of new anti-cancer therapy. In case of an event after 2 or more missed scans, censoring will be done at last adequate tumor assessment date before the missed scans (Censoring rule based on FDA guideline). Two scans are considered missing if no evaluable response result (CR, PR, SD or PD) is available within a period of 98 days (6+1 weeks times 2) for 1Q3W dose schedule and a period of 126 days (8+1 weeks times 2) for 3Q4W dose schedule.

15.1.5 Time to Confirmed Response according to RECIST 1.1 – Expansion Part

Time to Confirmed Response (TOR) is defined as the number of weeks from date of first IMP administration to the date of first response (CR or PR) according to RECIST 1.1. Only responders will be included in the analyses (no censoring). TOR will be analyzed using the

same statistical methodology as PFS. For these analyses, only confirmed responses will be used. Both the response assessments from the investigator will be presented.

The time to event graph of TOR will represent only confirmed responders and will start from the bottom-left corner (no responders) to the top-right corner.

15.1.6 Duration of Confirmed Response (RECIST 1.1) – Expansion Part

Duration of confirmed response (DoR) is defined as the number of weeks from the first documentation of confirmed objective tumor response (CR or PR) to the date of first PD or death. DoR will be analyzed using the same statistical methodology as PFS and the same censoring rules based on the FDA guideline, see section 15.1.4. DoR will be presented using confirmed responses only. Both the response assessments from the investigator will be presented.

15.1.7 Time to RECIST 1.1 and CA-125 combined response (Ovarian cancer only) – Expansion Part

Time to first RECIST 1.1 and CA-125 combined response (see Table 5 above) will be presented using the same statistical methodology as for ToR. CA-125 evaluation criteria (see section 15.1.2) should be fulfilled for CA-125 response evaluation, but not for RECIST 1.1 response evaluation (hence if they are NE based on CA-125, ovarian subjects are considered non-responder for CA-125 before defining the combined output). Both the response assessments from the investigator will be presented. The analysis will be performed for confirmed responses based on RECIST 1.1 only.

15.1.8 Events over Time – Expansion Part

Swimlane plots in which each lane documents the individual subject experience on a trial over time will be created for all confirmed responder subjects. The plots will include on-treatment, off-treatment periods, response according to RECIST 1.1 (investigator assessment), clinical progression and NLCB.

The no longer clinically benefitting (NLCB) reporting metric is defined as the date and the specific reason(s) a therapy was ultimately discontinued (end of treatment visit date).

15.2 Overall Survival

Overall survival is defined as the number of days from date of first IMP administration to death.

Overall survival will be presented using the same statistical methodology as for PFS except that censoring will not be applied neither when visits are skipped nor when new anti-cancer therapies are given. Subjects alive at the time of the analysis will be censored at minimum(cut-off date, last contact date).

The outputs will be repeated for the subgroups defined for cohorts 2 and 8 and for cohort 6 as mentioned in section 4.4.

15.3 Immunogenicity of Enapotamab Vedotin

Data on immunogenicity (anti-drug antibodies) of enapotamab vedotin will be listed only.

All details including presence of neutralizing antibodies (negative/positive) and titers of enapotamab vedotin will be listed.

[redacted]

15.4 Anti-tumor Activity

Anti-tumor activity measured by tumor shrinkage (based on sum of the diameter(s) of all target lesions from the CT-scan evaluations) as assessed by the investigators for the Expansion part will be listed and summarized graphically:

- graphical plots:
    - waterfall plots of the best percent change from baseline. The bars will be marked by the best overall response according to RECIST 1.1 based on investigator assessment for the dose-escalation part and based on investigator assessment for the expansion part
    - individual profiles plots: spider plots summarizing the percent change from baseline of the sum of diameter(s) of all target lesions marking the lines based on the best overall response according to RECIST 1.1 based on investigator assessment for the dose-escalation part and for the expansion part.

15.5 CA-125 (Ovarian cancer only)

Descriptive statistics (actual values, change from baseline and percent change from baseline) will be presented for the dose escalation and expansion part.

Mean-se plots over time will be done for the actual CA-125 values and percent change from baseline. In addition, individual subject's data (percent change from baseline) by visit and dose level/cohort will be plotted in an individual profiles plot.

Waterfall plots of the maximum decline in CA-125 that occurs at any point after treatment start will be presented. The bars will be marked by the best overall response according to RECIST 1.1 based on investigator assessment for the dose-escalation part and for the expansion part.

In the listing of CA-125 the CA-125 responses, RECIST 1.1 responses and combined RECIST 1.1 - CA-125 responses will be added.

15.6 PSA (Prostate cancer only) – Expansion Part

The PSA data, when available, will be listed only. The listing will also include PSA responses (>50% reduction, 3-4 weeks apart) and RECIST 1.1 -based responses.

15.7 Tumor Axl-Expression – Expansion Part

Tumor Axl-expression measurements will be listed and summarized descriptively (by tumor type, by fresh/archived biopsy, by last treatment given before the biopsy was taken based on pre-defined groups).

The following parameters will be included:

- H-score quantified based on Axl positivity in
    i) membrane,
    ii) cytoplasm,
    iii) membrane or cytoplasm (higher value of the two)

Descriptive statistics (actual values and percent change from baseline) will be presented to summarize the H-score parameters (for membrane and cytoplasm) at baseline and over time (archival and fresh screening results, cycle 2 and end–of-treatment results).

Mean-se plots over time will be done for the actual values and percent change from baseline.

[redacted]

Box-and-whisker plot showing baseline expression of Axl (H-score) across cohorts will also be presented.

15.8 [redacted]

[redacted]

16. Pharmacokinetics

The calculation of the pharmacokinetic endpoints will be performed by [redacted].

A separate PK analysis plan will be written by [redacted] to describe the planned non-compartmental PK analyses for this trial.

PK concentrations and individual PK parameters will be analyzed on the PK Analysis set.

Individual plasma/serum concentration time curves of enapotamab vedotin (conjugated), enapotamab vedotin (total) and free toxin (MMAE), including information on actual dose, will be presented for all subjects in the PK set for the escalation part. All available data will be shown in these figures. The value <LLoQ will be replaced by the numerical LLoQ value divided by 2 and mentioned in a footnote.

The plasma/serum concentrations will also be summarized descriptively over time according to the schedule specified in section 8.1 of the protocol final version 10.0, dd. 9 December 2019. The number of subjects with an imputed LLoQ value will be added.

Mean-se graphs for the plasma/serum concentrations by cycle and dose level will be presented both with and without error bars.

In addition, descriptive statistics will be calculated and presented for all individual PK parameters (Cmax, $AUC_{(0\text{-inf})}$, $AUC_{(0\text{-last})}$, CL, $T_{1/2}$ and T_{max}) for cycle 1 and cycle 3 for the dose-escalation part. This will include mean (arithmetic and/or geometric), median, min, max, n, standard deviation (SD), and geometric coefficient of variation (CV%) of the PK parameters of enapotamab vedotin (conjugated) , enapotamab vedotin (total) (only for the final analysis) and free toxin (MMAE) provided by [redacted]. Geometric mean and CV% will not be calculated for T_{max} and $T_{½}$.

Geometric CV% will be calculated as follows:

Geometric CV% = (sqrt(exp(variance for log transformed data)-1))*100

Mean-se graphs for the individual PK parameters (Cmax, $AUC_{(0\text{-inf})}$, $AUC_{(0\text{-last})}$, CL, $T_{1/2}$ and T_{max}) by cycle and dose level will be reported.

[redacted]

17. Safety Evaluation

All results will be presented on the safety set (SAF).

17.1 Extent of Exposure

For the expansion part, the number of doses received, the duration of exposure to enapotamab vedotin (days), the actual cumulative dose (mg), as well as the actual and relative dose intensities (continuous and in categories: >= 110%, 90% to < 110%, 70% to < 90%, 50% to < 70% , < 50%, missing) will be summarized by means of descriptive statistics using the safety set.

The duration of exposure to enapotamab vedotin (days) will also be presented by a Kaplan-Meier plot (without censoring).

Also, the number of subject days (total number of days in trial) will be presented by means of descriptive statistics for each dose/cohort group.

For the dose-escalation part, only the number of doses received, number of days in the trial and the duration of exposure will be presented as mentioned above.

17.2 Adverse Events

Summary tables for AEs described below will include only AEs that are treatment-emergent, i.e. AEs that started or worsened (taking into account the dates of grade changes) during the treatment period including the safety follow-up period.

Adverse events collected during the pre-treatment will be tabulated together with the medical history (by SOC and PT) and will be included in the serious AE listing (marked with a flag). Adverse events collected during the follow-up period will be tabulated separately from the treatment-emergent AEs and will be included in the AE listings (marked with a flag).

See section 4.1.1 for definition of pre-treatment, treatment and follow-up periods.

Missing or partial AE start date will be estimated in order to include events in summary tables in case of doubt (see section 4.7 for more details).

A summary table will present the number and percentage of subjects with at least one:

- Treatment-emergent adverse event (TEAE)
- TEAE related to enapotamab vedotin
- Infusion-related TEAE
- TEAE leading to permanent discontinuation of the trial treatment
- TEAE leading to drug interruption
- TEAE leading to dose reduction
- Serious TEAE
- Serious TEAE related to enapotamab vedotin
- Grade ≥3 serious TEAE
- Grade ≥3 serious TEAE related to enapotamab vedotin
- Fatal TEAE
- Fatal TEAE related to enapotamab vedotin

[redacted]

- Grade ≥3 TEAE
- Grade ≥3 TEAE related to enapotamab vedotin
- Grade ≥3 TEAE leading to permanent discontinuation of the trial treatment
- TEAE of special interest (AESI): constipation, neutropenia, peripheral neuropathy, vomiting, diarrhea, hyponatremia and possibly other types of adverse events[1]
- TEAE of special interest (AESI) leading to permanent discontinuation of the trial treatment: constipation, neutropenia, peripheral neuropathy, vomiting, diarrhea, hyponatremia and possibly other types of adverse events[2]
- Grade 1 TEAE of special interest by type
- Grade 2 TEAE of special interest by type
- Grade 3 TEAE of special interest by type
- Grade 4 TEAE of special interest by type
- Grade 5 (fatal) TEAE of special interest by type
- Medication errors and overdose TEAEs

The AE summary table will also be repeated for all subjects on 2.2 mg/kg across escalation and expansion, all subjects on 1.0 mg/kg across escalation and expansion, and all patients across escalation and expansion (i.e. three columns).

The following tabulations will be presented by PT (order by decreasing frequency), by SOC and PT (order by decreasing frequency of SOC and by decreasing frequency of PT within SOC) and by SOC or type, PT and highest NCI-CTCAE grade (order by decreasing frequency of SOC or type and by decreasing frequency of PT within SOC) as indicated:

- All TEAEs by PT
- Most frequent (20%) TEAEs by PT
- All TEAEs by SOC and PT
- All AEs during the follow-up period by SOC and PT and highest NCI-CTCAE grade
- All TEAEs by SOC and PT and highest NCI-CTCAE grade²
- TEAEs related to enapotamab vedotin by PT
- TEAEs related to enapotamab vedotin by SOC and PT
- TEAEs related to enapotamab vedotin by SOC and PT and highest NCI-CTCAE grade[3]
- NCI-CTCAE grade ≥3 TEAEs by PT
- Most frequent (5%) NCI-CTCAE grade ≥3 TEAEs by PT

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[1] AEs of special interest will be tabulated by AESI type. The AESI types will be defined using MedDRA SMQ lists or preferred term lists provided by sponsor at the time of the analysis programming.

[2] AEs of special interest will be tabulated by AESI type. The AESI types will be defined using MedDRA SMQ lists or preferred term lists provided by sponsor at the time of the analysis programming.

[3] Only most frequent AEs (> X% of Any Grade overall) will be included. The X% will be defined at the time of the analysis programming.

[redacted]

- NCI-CTCAE grade ≥3 TEAEs related to enapotamab vedotin by PT
- NCI-CTCAE grade ≥3 TEAEs by SOC and PT
- TEAEs leading to permanent discontinuation of the trial treatment by PT
- TEAEs leading to drug interruption by PT
- TEAEs leading to dose reduction by PT
- TEAEs of special interest by type and PT
- TEAEs of special interest by type and PT and highest NCI-CTCAE grade
- TEAEs of special interest related to enapotamab vedotin by type and PT
- NCI-CTCAE grade ≥3 TEAEs of special interest by type and PT
- Serious TEAEs of special interest by type and PT
- TEAEs of special interest leading to permanent discontinuation of the trial treatment by type and PT

In all tabulations, subjects will only be counted once for each preferred term. In case a subject experienced the same event more than once or has reported grade changes, the highest NCI-CTCAE grade will be presented.

In addition, time to onset of first AESI (for subjects with at least one event), total number of AESI events, total number and percentage of AESI events with outcome of resolution, and time to resolution of each AESI event (for events which are resolved) will be summarized by AESI type using descriptive statistics. AESI events with partial start date will be imputed accordingly to the rules described in section 4.7.

Time to onset of first AESI event will also be presented graphically by AESI type using a cumulative distribution function (one plot with one line for each AESI type); subjects with no AESI will not be included. This plot will also be presented for all subjects on 2.2 mg/kg across escalation and expansion and one for all subjects on 1.0 mg/kg across escalation and expansion.

For subjects with constipation, the number of subjects who did or didn't use prophylactic laxatives (based on diary data) will be tabulated.

For subjects with neutropenia, the number of subjects who did or didn't use G-CSF (based on concomitant medications) will be tabulated.

Treatment-emergent adverse events of special interest will also be presented in a table by type, cycle and preferred term and in a segmented bar-chart (each segment displays highest NCI-CTCAE grade with % of subjects who experience AESIs and related AESIs over time. Note: the % over time should be based on subjects still in the trial at the time of the corresponding cycle. When the same adverse event occurs more than once, only the first event will be included (similarity is defined based on the preferred term). Adverse events will be assigned to the cycle based on the onset date of this first AE. The highest NCI-CTCAE grade will take into account all occurrences of the same preferred term and all the individual grade changes as reported in the eCRF. The segmented bar-chart will also be produced for all subjects on 2.2 mg/kg across escalation and expansion and one for all subjects on 1.0 mg/kg across escalation and expansion.

Listings of all treatment-emergent adverse events will be provided including the subject identifier (including site and country), age, race, sex, verbatim, preferred term, duration of the event, highest NCI-CTCAE grade, reported NCI-CTCAE grade, grade changes and timing of grade changes, action taken, outcome, causality, date of onset, cycle of onset, date of resolution, days since the first dose, days since the last dose, serious (Y/N), DLT

[redacted]

(Y/N) for dose-escalation part, adverse event of special interest (Y/N) and infusion reaction (Y/N).

In addition, the most frequent adverse events will be presented in a segmented bar-chart for all subjects on 2.2 mg/kg across escalation and expansion and one for all subjects on 1.0 mg/kg across escalation and expansion.

17.3 Deaths, Serious and Other Significant Adverse Events

The number of deaths will be summarized in a table including all deaths, deaths in 30 days after last IMP administration, deaths in 100 days after last IMP administration and deaths after 100 days after last IMP administration, with a subgroup how many subjects died after last study date. The primary cause of death will be included in the listing.

Serious TEAEs, related serious TEAEs, serious TEAEs leading to permanent discontinuation of the trial treatment, serious AEs during follow-up period, fatal TEAEs and related fatal TEAEs will be summarized grouped by preferred term (order by decreasing frequency and by SOC or type, PT and highest NCI-CTCAE grade (order by decreasing frequency of SOC or type and by decreasing frequency of PT within SOC) as indicated:

- Serious TEAEs by PT
- Serious TEAEs related to enapotamab vedotin by PT
- Serious TEAEs leading to permanent discontinuation of the trial treatment by PT
- Serious TEAEs by SOC and PT and highest NCI-CTCAE grade
- Serious TEAEs related to enapotamab vedotin by SOC and PT and highest NCI-CTCAE grade
- Serious AEs during follow-up period by SOC and PT and highest NCI-CTCAE grade
- Fatal TEAEs by PT
- Fatal TEAEs related to enapotamab vedotin by PT

In addition, listings of serious AEs, fatal AEs and NCI-CTCAE grade ≥3 AEs will be provided, similarly to the listing of all AEs.

Adverse events related to the trial treatment and serious adverse events reported during the follow-up period will be presented by SOC and PT and highest NCI-CTCAE grade.

17.4 Subject Diary

The information from the subject diaries will be listed and summarized.

Number of subjects completing the diary overall and whether they have taken the prophylactic laxatives or not will be presented.

A table will be included presenting what was prescribed as prophylactic therapy based on the diary data.

[redacted]

17.5 Clinical Laboratory Data

The following laboratory parameters are measured:

- Biochemistry parameters: Sodium, potassium, magnesium, creatinine, calcium, blood urea nitrogen, AST, ALT, alkaline phosphatase, albumin, glucose, total bilirubin, lactate dehydrogenase, uric acid, C-reactive protein, lipase, amylase, gamma-glutamyl transferase, glycosylated hemoglobin, chloride, cholesterol, triglycerides, high-density lipoprotein and low density lipoprotein (calculated), thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4)
- Hematology parameters: Red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cell count with differential, platelet count and reticulocyte count
- Coagulation factors (prothrombin time, international normalized ratio and activated partial thromboplastin time).

Safety laboratory assessments (biochemistry, hematology and coagulation factors) will be graded using NCI-CTCAE version 4.03 if possible. All laboratory assessments will be converted to the corresponding international system of unit. If the values are within the normal ranges (for both local and central laboratory data), the grading will be overwritten by grade 0.

For uric acid, grade 1 and grade 3 are defined with overlapping boundaries: >ULN – 10 mg/dl (590 µmol/L); for grade 1 without physiologic consequences and for grade 3 with physiologic consequences (no grade 2). In all listings and tables (e.g. shift-tables based on NCI-CTCAE-grade) where uric acid is presented with NCI-CTCAE grade: a footnote will be added:

"A uric acid value >ULN-590 µmol/L is either NCI-CTCAE grade 1 if there is no physiological consequence or grade 3 if there is. In the absence of physiological consequence information and for the purpose of presentation in this listing/table/graph, such values are here considered to be grade 1".

Central laboratory results will be presented in shift tables and listed. Local laboratory results will be listed only.

Shift tables will be produced for all laboratory parameters graded by NCI-CTCAE grading. These tables will summarize the number of subjects with each baseline NCI-CTCAE grade and changes to the maximum NCI-CTCAE grade. For the calculation of the maximum NCI-CTCAE grade, both scheduled and unscheduled values available during the treatment period will be used.

For laboratory parameters that are not graded, shift tables based on normal ranges (low, high, normal) will be produced. These tables will summarize the number of subjects going from Normal/Low at baseline to High at any post-baseline, and going from Normal/High at baseline to Low at any post-baseline. Both scheduled and unscheduled values available during the treatment period will be used.

The number of subjects with at least one NCI-CTCAE grade 3 or grade 4 laboratory value during the treatment period will be summarized in a table overall and by laboratory parameter.

The following subject data listings will be produced for all laboratory parameters where NCI-CTCAE grades are defined:

- Listing of all laboratory abnormalities of NCI-CTCAE grade 3 or 4.

[redacted]

- Listing of all laboratory data including NCI-CTCAE grades (if applicable) as well as classifications relative to the laboratory reference ranges separated by central and local laboratory results.

All other laboratory parameters will be listed by subject, laboratory parameter and visit in the above second set of listings with grades left empty. Values outside the laboratory reference range will be flagged.

In addition, the frequency of subjects with incidence of drug induced liver laboratory abnormalities will be summarized descriptively and listed. Drug induced liver laboratory abnormalities will be defined as subjects meeting or exceeding one of the following predefined limits post-baseline:

- AST and/or ALT > 3xULN
- AST and/or ALT > 5xULN
- AST and/or ALT > 10xULN
- AST and/or ALT > 20xULN
- AST and/or ALT > 3xULN and Total Bilirubin > 2xULN;
- AST and/or ALT > 3xULN and Total Bilirubin > 2xULN and ALP < 1.5xULN.
- AST and/or ALT > 3xULN and INR > 1.5

Of note, total bilirubin, ALP and/or INR measurements concurrent or within 30 days subsequent to ALT/AST elevation will be included for the assessment of the incidence.

17.6 Other Safety Data

17.6.1 Vital Signs

Vital signs results will be listed with a flag marking the clinically notable values for each of the following parameters:

Clinically notable elevated values

- Systolic BP: >=180 mmHg and an increase >=20 mmHg from baseline
- Diastolic BP: >=105 mmHg and an increase >=15 mmHg from baseline.
- Weight: Increase from baseline of 10%
- Heart rate: >=120 bpm with increase from baseline of >=15 bpm
- Temperature: >38 °C

Clinically notable below normal values

- Systolic BP: <=90 mmHg and a decrease >=20 mmHg from baseline
- Diastolic BP: <=50 mmHg and a decrease >=15 mmHg from baseline
- Weight: decrease from baseline of >=10%
- Heart rate: <=50 bpm with decrease from baseline of >=15 bpm
- Temperature: <35 °C

The number of subjects with at least one clinically notable value as defined above will be summarized in a table.

[redacted]

17.6.2 Physical Findings

Baseline physical examination will be tabulated. All physical examination results will be listed.

Descriptive statistics (actual values and changes from baseline) over time will be given for body weight as it is important for the dosing.

17.6.3 ECG

ECG interpretation (Normal / Abnormal, not clinically significant, / Abnormal, clinically significant) and ECG measurements (RR, QT, QTcF, QTcB, PR and QRS) will be tabulated/summarized by visit and ECG time point (Before infusion, At the end of infusion, 2 hours after end of infusion, 5 hours after end of infusion). The three 12-lead ECG performed at each visit/time point will be combined as one measurement using the average of the three results (for ECG measurements), and the worst outcome of the three results for ECG interpretation.

Categorical analysis of QT, QTcB and QTcF interval data based on the number of subjects meeting or exceeding predefined limits in terms of absolute QT, QTcB and QTcF intervals (>450 ms or >480 ms or >500 ms) or changes from baseline (change of >30 ms or >60 ms) will be presented at baseline and at any post-baseline visit.

Additionally, categorical analysis of PR interval data based on the number of subjects meeting or exceeding predefined limits in terms of absolute PR (>200 ms or >220 ms) or changes from baseline (change of >25%) will also be presented at baseline and at any post-baseline visit.

Lastly, categorical analysis of QRS interval data based on the number of subjects meeting or exceeding predefined limits in terms of absolute QRS (>110 ms or >120 ms) or changes from baseline (change of >25%) will also be presented at baseline and at any post-baseline visit.

A listing of these subjects will be produced.

QTcB and QTcF will also be presented graphically using a mean-se plot over time for change from baseline values.

17.7 ECOG Performance Score

ECOG performance score assessments will be listed and summarized descriptively over time.

17.8 Hepatitis B, C and Cytomegalovirus Serology

All hepatitis B, C, and CMV serology data will be listed.

17.9 Pregnancy Test

Pregnancy test results will be tabulated presenting the number and percentage of subjects with at least one positive or borderline versus all negative. The positive or borderline results will be included per visit.

All pregnancy test data will be listed.

[redacted]

18. Exploratory Analyses [redacted]

[redacted]

[redacted]

Table 6. [redacted]

[redacted]

[redacted]

19. References

1. http://www.consort-statement.org/
2. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). European journal of cancer (Oxford, England: 1990). 2009;45(2):228-247.
3. Rustin GJ, Vergote I, Eisenhauer E, et al. Definitions for response and progression in ovarian cancer clinical trials incorporating RECIST 1.1 and CA-125 agreed by the Gynecological Cancer Intergroup (GCIG). International journal of gynecological cancer: official journal of the International Gynecological Cancer Society. 2011;21(2):419-423.
4. Scher HI, Morris MJ, Stadler WM, et al. Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. J Clin Oncol. Apr 202016; 34(12): 1402-1418.

[redacted]

20. List of Tables/Graphs/Listings

20.1 List of Statistical Tables

General	Dose-Escalation Part	Expansion Part
Table 14.01.01: Screen Failures	X	X
Table 14.01.02: Analysis Sets	X	X
Table 14.01.03.01: Subject Treatment Disposition	X	X
Table 14.01.03.02: Subject Study Disposition	X	X
Table 14.01.04: Important Major Protocol Deviations	X	X
Table 14.01.04.01: Covid-19 Protocol Deviations (if needed)	X	X
Table 14.01.05: Demographic Characteristics	X	X
Table 14.01.06: Baseline Disease Characteristics	X	X
Table 14.01.07: Biopsy Information	X	X
Table 14.01.08.01: Medical History (Ongoing) – by SOC and Preferred Term	X	X
Table 14.01.08.02: Medical History (Past) – by SOC and Preferred Term	X	X
Table 14.01.08.03: Surgical History – by SOC and Preferred Term	X	X
Table 14.01.09.01: Prior Cancer Therapies - Summary	X	X
Table 14.01.09.02: Prior Systemic Cancer Therapies – All – by ATC1 Name and ATC 4 Name	X	X
Table 14.01.09.03: Prior Treatment Lines of Systemic Cancer Therapies - by ATC1 Name and ATC 4 Name	X	X
Table 14.01.09.04: Prior Cancer Surgeries – by SOC and Preferred Term	X	X
Table 14.01.09.05: Prior Radiation Therapies – by SOC and Preferred Term	X	X
Table 14.01.10.01: Subsequent Systemic Cancer Therapies – by ATC1 Name and ATC 4 Name	X	X
Table 14.01.10.02: On-Study Cancer Surgeries – by SOC and Preferred Term	X	X
Table 14.01.10.03: On-Study Radiation Therapies – by SOC and Preferred Term	X	X
Table 14.01.11: Procedures – by SOC and Preferred Term	X	X
Table 14.01.12.01: Prior Medications – by ATC1 Name and ATC 4 Name	X	X
Table 14.01.12.02: Concomitant Medications – by ATC1 Name and ATC 4 Name	X	X
Table 14.01.12.03: Concomitant Medications for Blood Transfusion – by ATC1 Name and ATC 4 Name	X	X
Table 14.01.13: Baseline Physical Examinations	X	X
Efficacy Evaluation	**Dose-Escalation Part**	**Expansion Part**
Table 14.02.01.01: Response According to RECIST 1.1 – Investigator - Confirmed Responses	X	X
Table 14.02.01.02: Response According to RECIST 1.1 – Investigator – All Responses	X	X
Table 14.02.02: CA-125 Response	X	X
Table 14.02.03.01: Response According to RECIST 1.1 and CA-125 – Investigator - Confirmed Responses (Expansion Part only)		X
Table 14.02.03.02: Response According to RECIST 1.1 and CA-125 – Investigator - All Responses (Expansion Part only)		X
Table 14.02.04.01: Progression Free Survival According to RECIST 1.1 – Investigator	X	X
Table 14.02.04.02.xx: Progression Free Survival According to RECIST 1.1 by Subgroups – Investigator (Expansion Part only)		X
Table 14.02.05: Time to Confirmed Response According to RECIST 1.1 – Investigator (Expansion Part only)		X
Table 14.02.06: Duration of Confirmed Response According to RECIST 1.1– Investigator (Expansion Part only)		X
Table 14.02.07: Time to RECIST 1.1 and CA-125 Combined Response – Investigator - (Expansion Part only)		X
Table 14.02.08.01: Overall Survival	X	X
Table 14.02.08.02: Overall Survival by Subgroups (Expansion Part only)		X
Table 14.02.09: CA-125 – Descriptive Statistics	X	X
Table 14.02.10.a: H-Score in Membrane – Descriptive Statistics		X
Table 14.02.10.b: H-Score in Cytoplasm – Descriptive Statistics		X
Table 14.02.11: [redacted]	[redacted]	
Table 14.02.12.01: Peripheral Immune Phenotyping: neutrophils/lymphocytes – Descriptive Statistics		X

[redacted]

Table 14.02.12.02: Peripheral Immune Phenotyping: monocytes/lymphocytes – Descriptive Statistics		X
Pharmacokinetics	**Dose-Escalation Part**	**Expansion Part**
Table 14.02.13.01: Plasma/Serum Concentration of Enapotamab Vedotin (Conjugated, mg/L) – Descriptive Statistics	X	X
Table 14.02.13.02: Plasma/Serum Concentration of Enapotamab Vedotin (Total, mg/L) – Descriptive Statistics	X	X
Table 14.02.13.03: Plasma/Serum Concentration of Free Toxin (MMAE, ng/L) – Descriptive Statistics	X	X
Table 14.02.14.01: PK Parameters over Time - Enapotamab Vedotin (Conjugated) – Descriptive Statistics	X	
Table 14.02.14.02: PK Parameters over Time - Free Toxin (MMAE) – Descriptive Statistics	X	
Safety Evaluation	**Dose-Escalation Part**	**Expansion Part**
Table 14.03.01: Primary Endpoint: Summary of DLTs – Dose-Escalation Part	X	
Table 14.03.02: Enapotamab Vedotin Administration	X	X
Table 14.03.03.01: Summary of Adverse Events	X	X
Table 14.03.03.02: Summary of Adverse Events – 1.0 mg/kg and 2.2 mg/kg arms	X	X
Table 14.03.04.01.01: Treatment-Emergent Adverse Events - by PT	X	X
Table 14.03.04.01.02: Most Frequent (20%) Treatment-Emergent Adverse Events - by PT	X	X
Table 14.03.04.02: Treatment-Emergent Adverse Events - by SOC and PT	X	X
Table 14.03.04.03: Treatment-Emergent Adverse Events - by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.04.04: Adverse Events during Follow-up Period – by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.05.01: Enapotamab Vedotin Related TEAEs - by PT	X	X
Table 14.03.05.02: Enapotamab Vedotin Related TEAEs – by SOC and PT	X	X
Table 14.03.05.03: Enapotamab Vedotin Related TEAEs - by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.05.04: Enapotamab Vedotin Related Adverse Events during Follow-up Period – by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.06.01: NCI-CTCAE grade ≥3 TEAEs - by PT	X	X
Table 14.03.06.02: Most Frequent (5%) NCI-CTCAE grade ≥3 TEAEs - by PT	X	X
Table 14.03.06.03: NCI-CTCAE grade ≥3 TEAEs - by SOC and PT	X	X
Table 14.03.06.04: Enapotamab Vedotin Related NCI-CTCAE grade ≥3 TEAEs - by PT	X	X
Table 14.03.07.01: TEAEs Leading to Permanent Discontinuation of Trial Treatment - by PT	X	X
Table 14.03.07.02: TEAEs Leading to Drug Interruption of Trial Treatment - by PT	X	X
Table 14.03.07.03: TEAEs Leading to Dose Reduction of Trial Treatment - by PT	X	X
Table 14.03.08: TEAEs of Special Interest – Selection Criteria and SMQs	X	X
Table 14.03.08.01: TEAEs of Special Interest – by AESI Type and PT	X	X
Table 14.03.08.02: TEAEs of Special Interest – by AESI Type, PT and highest NCI-CTCAE Grade	X	X
Table 14.03.08.03: Enapotamab Vedotin Related TEAEs of Special Interest – by AESI Type and PT	X	X
Table 14.03.08.04: NCI-CTCAE grade ≥3 TEAEs of Special Interest – by AESI Type and PT	X	X
Table 14.03.08.05: Serious TEAEs of Special Interest – by AESI Type and PT	X	X
Table 14.03.08.06: TEAEs of Special Interest Leading to Permanent Discontinuation of Trial Treatment - by AESI Type and PT	X	X
Table 14.03.08.07: TEAEs of Special Interest by Cycle - by AESI Type and PT	X	X
Table 14.03.08.08: Time to Onset of First TEAE of Special Interest – by AESI Type, with Outcome of Resolution and Time to Resolution	X	X
Table 14.03.08.09: Constipation and Prophylactic Laxatives	X	X
Table 14.03.08.10: Neutropenia and Prophylactic G-CSF	X	X
Table 14.03.09.01: Serious TEAEs - by PT	X	X
Table 14.03.09.02: Enapotamab Vedotin Related Serious TEAEs - by PT	X	X
Table 14.03.09.03: Serious TEAEs Leading to Permanent Discontinuation of Trial Treatment - by PT	X	X

[redacted]

Table 14.03.09.04: Serious Adverse Events – by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.09.05: Enapotamab Vedotin Related Serious Adverse Events – by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.09.06: Serious Adverse Events during Follow-up Period – by SOC and PT and highest NCI-CTCAE Grade	X	X
Table 14.03.10.01: Fatal TEAEs - by PT	X	X
Table 14.03.10.02: Enapotamab Vedotin Related Fatal TEAEs - by PT	X	X
Table 14.03.11: Deaths	X	X
Table 14.03.12: Subject Diary Data including Prophylactic Laxatives	X	X
Table 14.03.13.xx: Biochemistry Laboratory Results - Shift Table from Baseline NCI-CTCAE Grade to Highest Post-Baseline NCI-CTCAE Grade	X	X
Table 14.03.14.xx: Biochemistry Laboratory Results - Shift table from Baseline to Maximum/Minimum Post-Baseline Abnormality	X	X
Table 14.03.15.xx: Hematology Laboratory Results - Shift Table from Baseline NCI-CTCAE Grade to Highest Post-Baseline NCI-CTCAE Grade	X	X
Table 14.03.16.xx: Hematology Laboratory Results - Shift table from Baseline to Maximum/Minimum Post-Baseline Abnormality	X	X
Table 14.03.17.xx: Coagulation factors Laboratory Results - Shift Table from Baseline NCI-CTCAE Grade to Highest Post-Baseline NCI-CTCAE Grade	X	X
Table 14.03.18.xx: Coagulation factors Laboratory Results - Shift table from Baseline to Maximum/Minimum Post-Baseline Abnormality	X	X
Table 14.03.19: NCI-CTCAE Grade 3/4 Laboratory Results	X	X
Table 14.03.20: Subject Incidence of Drug Induced Liver Laboratory Abnormalities	X	X
Table 14.03.21: Vital Signs Abnormalities	X	X
Table 14.03.22: Body Weight over Time - Descriptive Statistics	X	X
Table 14.03.23.01: ECG Measurements over Time – Descriptive Statistics	X	X
Table 14.03.23.02: ECG Abnormalities over Time	X	X
Table 14.03.24: ECOG Performance Score over Time	X	X
Table 14.03.25: Pregnancy Test Results over Time	X	X
Exploratory	**Dose-Escalation Part**	**Expansion Part**
Table 14.04.01.01.a: [redacted]	[redacted]	
Table 14.04.01.01.b: [redacted]		
Table 14.04.01.02.a: [redacted]		
Table 14.04.01.02.b: [redacted]		
Table 14.04.01.03.a: [redacted]		
Table 14.04.01.03.b: [redacted]		
Table 14.04.02.01: [redacted]		
Table 14.04.02.02: [redacted]		
Table 14.04.02.03: [redacted]		

* Only most frequent AEs (> X% of Any Grade overall) will be included. The X% will be defined at the time of the analysis programming.

[redacted]

20.2 List of Graphs

General	Dose-Escalation Part	Expansion Part
Graph 14.01.01: [redacted]		
Efficacy Evaluation	**Dose-Escalation Part**	**Expansion Part**
Graph 14.02.01.01: Response According to RECIST 1.1 – Subgroup Analysis – Investigator (Expansion Part only)		X
Graph 14.02.01.02: Clinical Benefit at week 12/16 – Subgroup Analysis – Investigator (Expansion Part only)		X
Graph 14.02.02.01: PFS According to RECIST 1.1 – Kaplan-Meier Curves– Investigator	X	X
Graph 14.02.02.02.xx: PFS According to RECIST 1.1 – Kaplan-Meier Curves - Subgroup Analysis – Investigator (Expansion Part only)		X
Graph 14.02.03: Time to Confirmed Response according to RECIST 1.1 – Investigator (Expansion Part only)		X
Graph 14.02.04: DoR According to RECIST 1.1 – Kaplan-Meier Curves – Investigator (Expansion Part only)		X
Graph 14.02.05: Time to RECIST 1.1 and CA-125 Combined Response – Kaplan-Meier Curves – Investigator (Expansion Part only)		X
Graph 14.02.06: Events over Time		X
Graph 14.02.07.01: Overall Survival – Kaplan-Meier Curves	X	X
Graph 14.02.07.02.xx: Overall Survival – Kaplan-Meier Curves - Subgroup Analysis		X
Graph 14.02.08.01.xx: Tumor Shrinkage: Percent Change in Tumor Size Compared to Baseline – Investigator - Individual Profiles	X	X
Graph 14.02.08.02.xx: Tumor Shrinkage: Best Percent Change in Tumor Size Compared to Baseline – Investigator	X	X
Graph 14.02.09.01: CA-125: Actual Values	X	X
Graph 14.02.09.02: CA-125: Percent Change from Baseline	X	X
Graph 14.02.09.03.xx: CA-125: Percent Change from Baseline - Individual Profiles	X	X
Graph 14.02.09.04: Best Percent Change in CA-125 Marked with Best Overall Response - Investigator	X	X
Graph 14.02.10.01.a: [redacted]		
Graph 14.02.10.01.b: [redacted]		
Graph 14.02.10.02.a: [redacted]		
Graph 14.02.10.02.b: [redacted]		
Graph 14.02.10.03.a: [redacted]		
Graph 14.02.10.03.b: [redacted]		
Graph 14.02.11.01: [redacted]		
Graph 14.02.11.02: [redacted]		
Graph 14.02.11.03: [redacted]		
Graph 14.02.12: [redacted]		
Pharmacokinetics	**Dose-Escalation Part**	**Expansion Part**
Graph 14.02.13.01: Plasma/Serum Concentration of Enapotamab Vedotin (Conjugated) – PK Profiles – Dose-Escalation Part	X	X
Graph 14.02.13.02: Plasma/Serum Concentration of Enapotamab Vedotin (Total) – PK Profiles- – Dose-Escalation Part	X	X
Graph 14.02.13.03: Plasma/Serum Concentration of free toxin (MMAE) – PK Profiles – Dose-Escalation Part	X	X
Graph 14.02.14.01: Plasma/Serum Concentration of Enapotamab Vedotin (Conjugated)	X	X
Graph 14.02.14.02: Plasma/Serum Concentration of Enapotamab Vedotin (Total)	X	X
Graph 14.02.14.03: Plasma/Serum Concentration of free toxin (MMAE)	X	X
Graph 14.02.15.01.xx: PK Parameters of Enapotamab Vedotin (Conjugated) - <PK Parameter >	X	
Graph 14.02.15.02.xx: PK Parameters of Free Toxin (MMAE) - <PK Parameter >	X	

[redacted]

Safety Evaluation	Dose-Escalation Part	Expansion Part
Graph 14.03.01: Summary of DLTs – Dose-Escalation Part	X	
Graph 14.03.02: Duration of Exposure - Kaplan-Meier Curves	X	X
Graph 14.03.03: Time to First TEAE of Special Interest	X	X
Graph 14.03.04: TEAEs of Special Interest by Cycle and AESI Type – Bar Charts	X	X
Graph 14.03.04: TEAEs of Special Interest by Cycle and AESI Type – Bar Charts	X	X
Exploratory	**Dose-Escalation Part**	**Expansion Part**
Graph 14.04.01.01.a: [redacted]	[redacted]	
Graph 14.04.01.01.b: [redacted]		
Graph 14.04.01.02.a: [redacted]		
Graph 14.04.01.02.b: [redacted]		
Graph 14.04.02.01.a: [redacted]		
Graph 14.04.02.01.b: [redacted]		
Graph 14.04.02.02.a: [redacted]		
Graph 14.04.02.02.b: [redacted]		
Graph 14.04.02.03.a: [redacted]		
Graph 14.04.02.03.b: [redacted]		
Graph 14.04.03.01: [redacted]		
Graph 14.04.03.02: [redacted]		
Graph 14.04.03.03: [redacted]		
Graph 14.04.04.01.a: [redacted] or		
Graph 14.04.04.01.b: [redacted]		
Graph 14.04.04.02.a: [redacted]		
Graph 14.04.04.02.b: [redacted]		
Graph 14.04.05.03.a: [redacted]		
Graph 14.04.05.03.b: [redacted]		
Graph 14.04.06.01: [redacted]		
Graph 14.04.06.02: [redacted]		
Graph 14.04.06.03: [redacted]		
Graph 14.04.07.a: [redacted]		
Graph 14.04.07.b: [redacted]		
Graph 14.04.08.a: [redacted]		
Graph 14.04.08.b: [redacted]		
Graph 14.04.09.a: [redacted]		
Graph 14.04.09.b: [redacted]		

[redacted]

20.3 List of Derived Data Listings

All available data has to be included in the listings.

General
Listing 16.02.01.01: Screening Failures and Not-treated Subjects
Listing 16.02.01.02: Subject Disposition
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Listing 16.02.01.03.01: Covid 19 Protocol Deviations - All important PDs related to Covid-19
Listing 16.02.01.03.02: Covid-19 Protocol Deviations - All non-important PDs related to Covid-19
Listing 16.02.01.03.03: Covid-19 Protocol Deviations - Subject listing of missed/changed visits
Listing 16.02.01.03.04: Covid-19 Protocol Deviations - Subject listing of assessments missed due to visits impacted by Covid-19
Listing 16.02.01.04: In- and Exclusion Criteria not met
Listing 16.02.01.05: Demographic Characteristics
Listing 16.02.01.06: Baseline Disease Characteristics
Listing 16.02.01.07: Biopsy Information
Listing 16.02.01.08: Medical and Surgical History including Pre-Treatment Adverse Events
Listing 16.02.01.09: Prior Cancer Therapies
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Efficacy Evaluation
Listing 16.02.02.01: Target, Non-target and New Lesions Information (Including all Assessments) – Investigator Assessments
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Listing 16.02.02.02.02: Response Information (Including BOR and CBOR) – IRC Assessments
Listing 16.02.02.03: CA-125 Values and CA-125 Response (Including Time to Response)
Listing 16.02.02.04: PSA Values and PSA Response
Listing 16.02.02.05: Immunogenicity of Enapotamab Vedotin
Listing 16.02.02.06: Tumor Axl-Expression
Pharmacokinetics
Listing 16.02.02.07: Plasma/Serum Concentration of Enapotamab Vedotin (Conjugated), Enapotamab Vedotin (Total) and Free Toxin (MMAE)
Listing 16.02.02.08: PK Parameters of Enapotamab Vedotin (Conjugated), Enapotamab Vedotin (Total) and Free Toxin (MMAE)
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Listing 16.02.03.09: Adverse Events of Special Interest
Listing 16.02.03.10: Deaths
Listing 16.02.03.11: Subject Diary Data
Listing 16.02.03.12: NCI-CTCAE Grade 3/4 Laboratory Results
Listing 16.02.03.13.01: Laboratory Results – Central Laboratory Results
Listing 16.02.03.13.02: Laboratory Results – Local Laboratory Results
Listing 16.02.03.14: Physical Examination Results
Listing 16.02.03.15: Visual Acuity
Listing 16.02.03.16: ECG Results
Listing 16.02.03.17: Vital Signs
Listing 16.02.03.18: ECOG Performance Score
Listing 16.02.03.19: Hepatitis B, C and Cytomegalovirus Serology
Listing 16.02.03.20: Pregnancy Data

Section Number	Title
Section 21	Version history

Pages 46-47 removed - **Out of Scope**

Signature Page for GCT1021-01_SAP_Addendum
Study GCT1021-01 v1.0

eSignature for Approval	[redacted] Author 22-Feb-2022 11:57:13 GMT+0000
eSignature for Approval	[redacted] Sponsor 22-Feb-2022 14:35:06 GMT+0000
eSignature for Approval	[redacted] Sponsor 22-Feb-2022 14:39:17 GMT+0000
eSignature for Approval	[redacted] [redacted] Statistician 22-Feb-2022 14:49:08 GMT+0000

Signature Page for GCT1021-01_SAP_Addendum
Study GCT1021-01 v1.0

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Statistical Analysis Plan – Addendum

Sponsor:	Genmab
Protocol Title:	First-in-human, open-label, dose-escalation trial with expansion cohorts to evaluate safety of Axl-specific antibody-drug conjugate (enapotamab vedotin, HuMax®-AXL-ADC) in subjects with solid tumors
Protocol Version:	Final version 11.0, dd. 30 June 2021
Trial Code:	GCT1021-01

[redacted]

Author: [redacted] Biostatistician

Reviewer: [redacted], Biostatistical Services

For Sponsor:

Reviewers:

- [redacted] Biostatistics (Approver)
- [redacted] Medical [redacted] (Approver)
- [redacted], Global Drug Safety Pharmacovigilance Physician
- [redacted]
- [redacted] Pharmacology
- [redacted] Biostatistics
- [redacted], Global Drug Safety and Pharmacovigilance
- [redacted] Programming [redacted].
- [redacted], Medical Writer
- [redacted], Biostatistics

TPL N°: eTPL SA-02-01 TPL Version: 02
Of SOP SA-02.08
TPL Effective Date: 31 Mar 2016
Approved in Vault: 22 Feb 2022

[redacted]

Table of Contents

[redacted]

1. List of Abbreviations and Definition of Terms

See SAP version 4 dd. 30 June 2021.

2. Introduction

This Statistical Analysis Plan Addendum is written for the clinical trial GCT1021-01 conducted in Denmark, Belgium, UK, US, the Netherlands, and Spain (the last two added for the expansion part of the trial). The ICH guideline E3 "Structure and Content of Clinical Study Reports" is used as a guide to the writing of the plan.

In November 2020, Genmab decided to discontinue development of enapotamab vedotin but continue to offer treatment to patients who are deriving clinical benefit in the present trial. With Protocol Amendment 10, procedures and visits are reduced for the 3 remaining patients active on trial treatment. For patients still in follow-up *(survival follow-up, ie the time period between end of treatment period (date of last IMP + 30 days) until death)*, (n=47) the survival status will be collected once before final cessation follow-up following the implementation of this Protocol Amendment 10. This SAP addendum describes the analyses of the data collected until the end of the trial. This SAP addendum does not replace the previous versions but is complementary to the SAP version 4 (amendment 3) dd. 30 June 2021.

2.1 Planned Analyses

Data collected up to and including the data cut-off date *of 22 March 2021 has been reported in the* CSR as per SAP version 4 dd. 30 June 2021. Data collected after the 22 March 2021 data cut-off date until the end of trial (last patient end of safety follow-up on 12 November 2021) will be reported in an addendum to the CSR based on the reporting described in this SAP addendum. *This reporting in the addendum to the CSR includes data from the 3 subjects who remained on treatment after 22 March 2021 as well as data from the 47 subjects who remained in the (survival) follow-up period after 22 March 2021.*

Populations will be defined as described in the SAP version 4 dd. 30 June 2021. Programs from the main analyses will be reused with the same definitions and decision rules except for the definition of what constitute an AESI in the CSR Addendum.

Following outputs will be repeated from the main analyses:

- Subject disposition
- Progression free survival
- Overall survival
- TEAE by PT
- Drug-induced liver injury
- All listings of all data after the cut-off date of 22 March 2021

The following output will be added

- Time to onset of first TEAE (AESI only),
- Time to resolution (AESI only); with percentage of events with outcome of resolution
- Time to improvement of TEAE (AESI only), percentage of events with improvement; with percentage of events with improvement
- AE summary table – (same categories as in the main CSR but with the AESI categories as described below and AESI leading to permanent discontinuation of the trial treatment added)
- TEAE by PT and maximum grade
- TEAE of special interest – by AESI type and PT

[redacted]

- TEAE of special interest – by AESI type, PT and highest NCI-CTCAE Grade
- Enapotamab Vedotin Related TEAEs of Special Interest - by AESI Type and PT
- NCI-CTCAE grade >= 3 TEAEs of Special Interest - by AESI Type and PT
- Serious TEAEs of Special Interest - by AESI Type and PT
- TEAEs of Special Interest Leading to Permanent Discontinuation of Trial Treatment - by AESI Type and PT

The definition of AESI in the CSR Addendum:

- PN: AEs with PTs within the peripheral neuropathy MedDRA SMQ: Peripheral neuropathy SMQ [20000034] (Broad)
- Constipation: PT
- Neutropenia: PTs neutropenia, neutrophil count decreased and febrile neutropenia.

Note: As "Immune related Adverse Events", which is generally associated with immune checkpoint inhibitors, didn't result in clinically significant findings in this study, its relevance is not applicable thus will not be included in the above AESI table.

All derived dataset programs will rerun on the whole database and contain all data. A flag marking new records and changed records will be added to each derived dataset.

3. Additional outputs

All available data from the start of the trial until the end of the trial will be included in the selected tables and graphs for all patients in the study.

3.1 Disposition of Subjects

The frequency of subjects treated, of subjects who discontinued the trial treatment and of subjects who terminated the trial will be given for the full analysis set (FAS). The primary reason for discontinuation of the trial treatment and terminating the trial will be summarized. The details of the 'other reason' will be included in the listing.

3.2 PFS and Overall Survival

PFS is defined as the number of days from the date of first IMP administration to first PD or death whichever occurs first.

PFS will be presented using the same statistical methodology as described in the SAP version 4 dd. 30 June 2021.

Overall survival is defined as the number of days from date of first IMP administration to death.

Overall survival will be presented using the same statistical methodology as for PFS (see SAP version 4 dd. 30 June 2021) except that censoring will not be applied neither when visits are skipped nor when new anti-cancer therapies are given. Subjects alive at the time of the analysis will be censored at minimum(cut-off date, last contact date).

[redacted]

3.3 Adverse Events Summary Table

A summary table for AEs described below will include only AEs that are treatment-emergent, i.e. AEs that started or worsened (taking into account the dates of grade changes) during the treatment period including the safety follow-up period.

The summary table will present the number and percentage of subjects with at least one:

- Treatment-emergent adverse event (TEAE)
- TEAE related to enapotamab vedotin
- Infusion-related TEAE
- TEAE leading to permanent discontinuation of the trial treatment
- TEAE leading to drug interruption
- TEAE leading to dose reduction
- Serious TEAE
- Serious TEAE related to enapotamab vedotin
- Grade ≥3 serious TEAE
- Grade ≥3 serious TEAE related to enapotamab vedotin
- Fatal TEAE
- Fatal TEAE related to enapotamab vedotin
- Grade ≥3 TEAE
- Grade ≥3 TEAE related to enapotamab vedotin
- Grade ≥3 TEAE leading to permanent discontinuation of the trial treatment
- TEAE of special interest (AESI)
- TEAE of special interest (AESI) leading to permanent discontinuation of the trial treatment

AEs of special interest will be tabulated by AESI type (as defined in section 2.1).

The AE summary table will also be repeated for all subjects on 2.2 mg/kg across escalation and expansion, all subjects on 1.0 mg/kg across escalation and expansion, and all patients across escalation and expansion (i.e. three columns).

3.4 Time to onset of first AESI

Time to onset of first AESI (for subjects with at least one event), total number of AESI events will be summarized by AESI type using descriptive statistics. AESI events with partial start date will be imputed accordingly to the rules described in section 4.7 in the SAP version 4 dd. 30 June 2021.

Time to onset is presented by AESI type for the three searches specified in section 2.1.

3.5 Time to resolution of AESI

Time to resolution (AESI only); with percentage of events with outcome of resolution will be summarized by AESI type using descriptive statistics. AESI events with partial start date will be imputed accordingly to the rules described in section 4.7 in the SAP version 4 dd. 30 June 2021.

Time to resolution is presented by AESI type for the three searches specified in section 2.1.

[redacted]

3.6 Time to improvement of AESI

Improvement is defined as a change in severity to a lower grade.

Total number and percentage of AESI events with improvement and time to improvement of each AESI event (for events which are improved) will be summarized by AESI type using descriptive statistics. AESI events with partial start date will be imputed accordingly to the rules described in section 4.7 in the SAP version 4 dd. 30 June 2021.

Time to improvement is presented by AESI type for the three searches specified in section 2.1.

3.7 Adverse event tables by pt and/or soc and/or maximum grade

- TEAE by PT
- TEAE by PT and maximum grade
- TEAE of special interest – by AESI type and PT
- TEAE of special interest – by AESI type, PT and highest NCI-CTCAE Grade
- Enapotamab Vedotin Related TEAEs of Special Interest - by AESI Type and PT
- NCI-CTCAE grade >= 3 TEAEs of Special Interest - by AESI Type and PT
- Serious TEAEs of Special Interest - by AESI Type and PT
- TEAEs of Special Interest Leading to Permanent Discontinuation of Trial Treatment - by AESI Type and PT

3.8 Drug-induced liver injury

The frequency of subjects with incidence of drug induced liver laboratory abnormalities will be summarized descriptively and listed. Drug induced liver laboratory abnormalities will be defined as subjects meeting or exceeding one of the following predefined limits post-baseline:

- AST and/or ALT > 3xULN
- AST and/or ALT > 5xULN
- AST and/or ALT > 10xULN
- AST and/or ALT > 20xULN
- AST and/or ALT > 3xULN and Total Bilirubin > 2xULN
- AST and/or ALT > 3xULN and Total Bilirubin > 2xULN and ALP < 1.5xULN
- AST and/or ALT > 3xULN and INR > 1.5

Of note, total bilirubin, ALP and/or INR measurements concurrent or within 30 days subsequent to ALT/AST elevation will be included for the assessment of the incidence.

[redacted]

4. List of Tables/Graphs/Listings

4.1 List of Statistical Tables and Graphs

General	**Template***
Table A.14.01.01: Subject Treatment Disposition	Template 3
Table A.14.01.02: Subject Study Disposition	Template 4
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Table A 14.02.01: PFS	Template 18
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Table A.14.03.14: Subject Incidence of Drug Induced Liver Laboratory Abnormalities	Template 35

*Reference: SAP Mocks version 2, dd. 11February 2020

4.2 List of Derived Data Listings

All available data starting from the cut-off date of 22 March 2021 (excluded) until the end of the trial has to be included in the listings for all patients in the study.

General
Listing A.16.02.01.01: Screening Failures and Not-treated Subjects
Listing A.16.02.01.02: Subject Disposition
Listing A.16.02.01.03: Protocol Deviations
Listing A.16.02.01.03.01: Covid-19 Protocol Deviations - All important PDs related to Covid-19
Listing A.16.02.01.03.02: Covid-19 Protocol Deviations - All non-important PDs related to Covid-19
Listing A.16.02.01.03.03: Covid-19 Protocol Deviations - Subject listing of missed/changed visits
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Listing A.16.02.01.04: In- and Exclusion Criteria not met
Listing A.16.02.01.05: Demographic Characteristics
Listing A.16.02.01.06: Baseline Disease Characteristics
Listing A.16.02.01.07: Biopsy Information
Listing A.16.02.01.08: Medical and Surgical History including Pre-Treatment Adverse Events
Listing A.16.02.01.09: Prior Cancer Therapies
Listing A.16.02.01.10: Subsequent Cancer Therapies
Listing A.16.02.01.11: Procedures
Listing A.16.02.01.12.01: Prior Medications
Listing A.16.02.01.12.02: Concomitant Medications
Efficacy Evaluation
Listing A.16.02.02.01: Target, Non-target and New Lesions Information (Including all Assessments) – Investigator Assessments
Listing A.16.02.02.02.01: Response Information (Including BOR, PFS, DoR, TOR, OS) – Investigator Assessments

[redacted]

Listing A.16.02.02.02.02: Response Information (Including BOR and CBOR) – IRC Assessments
Listing A.16.02.02.03: CA-125 Values and CA-125 Response (Including Time to Response)
Listing A.16.02.02.04: PSA Values and PSA Response
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Listing A.16.02.02.06: Tumor Axl-Expression
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Listing A.16.02.02.07: Plasma/Serum Concentration of Enapotamab Vedotin (Conjugated), Enapotamab Vedotin (Total) and Free Toxin (MMAE)
Listing A.16.02.02.08: PK Parameters of Enapotamab Vedotin (Conjugated), Enapotamab Vedotin (Total) and Free Toxin (MMAE)
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Listing A.16.02.03.11: Subject Diary Data
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Listing A.16.02.03.16: ECG Results
Listing A.16.02.03.17: Vital Signs
Listing A.16.02.03.18: ECOG Performance Score
Listing A.16.02.03.19: Hepatitis B, C and Cytomegalovirus Serology
Listing A.16.02.03.20: Pregnancy Data

5. Version history

Version of the SAP addendum and date	Changes
Final version 1.0, 22Feb2022	Addendum to the SAP describing the analysis of data collected after the cut-off date of the main analysis until the end of the trial based on Protocol version 11, amendment 10 dd. 30 June 2021.