STATISTICAL ANALYSIS PLAN

Protocol XPORT-CRC-041

A Phase 2 Open-Label Multicenter Study to Evaluate the Safety and Efficacy of Selinexor with or without Pembrolizumab versus Standard of Care in Previously treated Metastatic Colorectal Cancer with RAS mutations

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Version	Date	Author(s)	Brief Summary of Changes
1.0	23 Mar 2023	PPD PhD.	Original based on PV 2.0

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	adverse event
BID	twice daily
BOR	best overall response
C	cycle
CI	confidence interval
CR	complete response
CRC	colorectal cancer
CTCAE	Common Terminology Criteria for Adverse Events
D	day
DCR	disease control rate
dMMR	deficient mismatch repair
CCI [redacted]	
DOR	duration of response
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EOT	end of treatment
HR	hazard ratio
ITT	intent to treat
IV	intravenous(ly)
MedDRA	Medical Dictionary for Regulatory Activities
MSI-H	microsatellite instability-high
NCI	National Cancer Institute
ORR	objective response rate
PD	progressive disease
CCI [redacted]	
PFS	progression-free survival
PO	orally
PR	partial response
QW	once weekly
RAS	rat sarcoma
RECIST	Response Evaluation Criteria in Solid Tumors

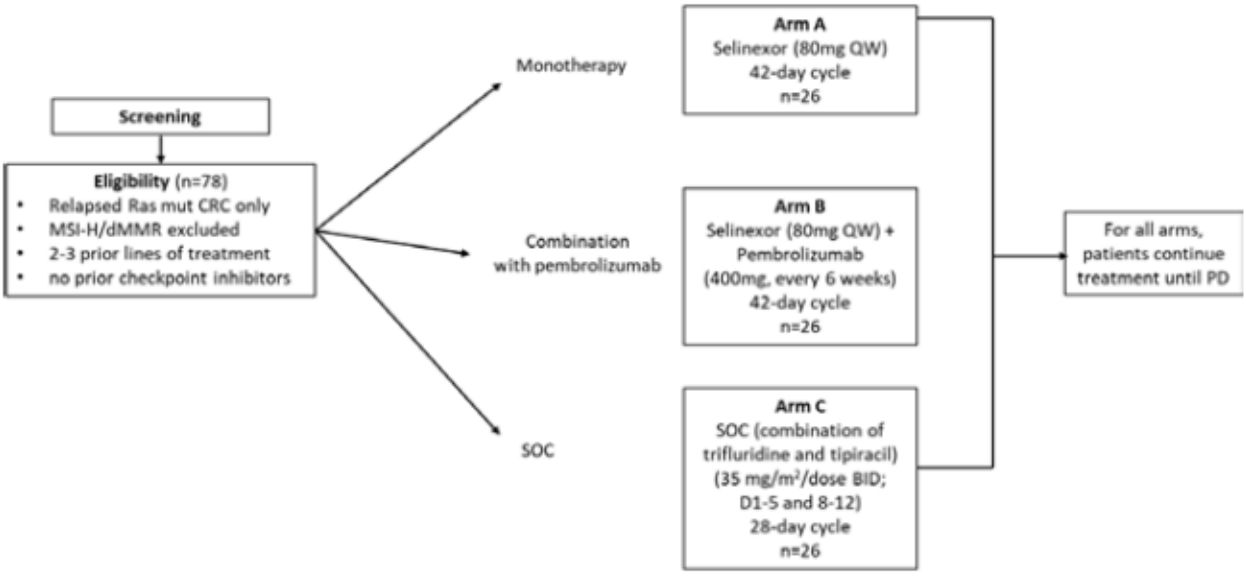
Abbreviation	Definition
CCI	[redacted]
SAE	serious adverse event
SAP	statistical analysis plan
SI	International System of Units
SOA	schedule of assessments
SOC	standard of care
SOC	system organ class
TEAE	treatment-emergent adverse event
TRAE	treatment-emergent treatment-related adverse event
WHO DDE	World Health Organization Drug Dictionary Enhanced

1. OVERVIEW AND INVESTIGATIONAL PLAN

1.1. OVERALL DESIGN

This is a phase 2, open-label, multicenter study that will evaluate the efficacy and safety of selinexor and pembrolizumab in patients with advanced or metastatic CRC. The study schema is depicted in **Error! Reference source not found.**.

Figure 1 Study Schema



SOC = Standard of care, PD = progressive disease; MSI-H = microsatellite instability high; dMMR = deficient mismatch repair; QW = once weekly; BID=twice daily; CRC=colorectal cancer

Approximately 78 patients with advanced or metastatic CRC will be enrolled, and randomized to Arm A, B or C based on the following stratification factor:

CCI [redacted]

All eligible patients in Arm A will be treated with selinexor 80 mg QW orally as a monotherapy on Day 1 of each week of a 42-day cycle. Arm B patients will be treated with selinexor at the same dose as Arm A in combination with pembrolizumab 400 mg IV once every 6 weeks. Arm C patients will be administered the standard of care treatment trifluridine and tipiracil 35 mg/m^2/dose orally BID (max 80 mg / dose) on Days 1 through 5 and Days 8 through 12 of each 28-day cycle. Trifluridine and tipiracil should be taken with food.

Primary efficacy will be assessed by PFS, as assessed by the investigator per RECIST1.1 for selinexor plus pembrolizumab and for SOC assessed from randomization until disease progression or death from any cause, whichever occurs first. Objective response rate (ORR) defined as the proportion of patients who achieve complete response (CR) or partial response (PR), per RECIST 1.1 as defined by the

Investigator based on radiologic criteria. Assessments will be performed per timepoints as mentioned in the schedule of assessments (SoA) in the protocol.

Safety and tolerability of study treatment will be evaluated based on AE reports by the occurrence, nature, and severity of AEs as categorized by the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Timepoints will be performed as mentioned in the SoA.

Patients will receive study treatment until disease progression (PD), intolerable toxicity, or withdrawal from the study. Disease response/progression will be based on tumor assessments at timepoints specified in the SoA.

1.2. STUDY OBJECTIVES AND ENDPOINTS

The following objectives will be assessed in patients with RAS mutated mCRC:

Table 1-1 Study Objectives and Endpoints

Objectives	Endpoints
Primary	
• To evaluate preliminary anti-tumor activity of selinexor with pembrolizumab versus standard of care (SOC)	• Progression-free survival (PFS), as assessed by the investigator per RECIST1.1 assessed from randomization until disease progression or death from any cause, whichever occurs first
Secondary	
• To evaluate preliminary anti-tumor activity of selinexor with pembrolizumab versus SOC	• Overall survival (OS), defined as time to death due to any cause from the randomization date • ORR, defined as the proportion of patients who achieve complete response (CR) or partial response (PR), per RECIST 1.1 as defined by the Investigator based on radiologic criteria • DCR is defined as the proportion of patients who have best response of PR or better, or at least 12 continuous weeks of SD before disease progression or initiating a new antineoplastic treatment. • PFS at 6 months, OS percent in 6 months, OS percent in 12 months, DOR, and DCR per RECIST 1.1

• To evaluate preliminary anti-tumor activity of selinexor only versus SOC	• Overall survival (OS), defined as time to death due to any cause from the randomization date • ORR, defined as the proportion of patients who achieve complete response (CR) or partial response (PR), per RECIST 1.1 as defined by the Investigator based on radiologic criteria • PFS at 6 months, OS percent in 6 months, OS percent in 12 months, DOR, and DCR per RECIST 1.1 • Progression-free survival (PFS) per RECIST 1.1 assessed by the investigator from the randomization date
• To describe the safety and tolerability of selinexor with and without pembrolizumab	• Safety and tolerability of study treatment will be evaluated based on AE reports by the occurrence, nature, and severity of AEs as categorized by the Common Terminology Criteria for Adverse Events (CTCAE) v5.0
Exploratory	
CCI	

CCI

[redacted]

1.3. DETERMINATION OF SAMPLE SIZE

CCI

[redacted]

Given above assumptions, the total sample size is approximately 78 patients with 26 in each arm.

1.4. STUDY PLAN

For each patient that signs the informed consent, the study consists of:

- Screening/baseline visit: occurs within 21 days prior to receiving the 1st dose of study treatment
- Treatment period: There is no maximum treatment duration. Treatment cycles of arm A and B last 42 days and arm C last 28 days. Patients may continue to receive study drugs until the patient has confirmed PD, withdraws consent, is lost to follow-up, experiences intolerable toxicity which precludes further treatment, or treatment is discontinued at the discretion of the patient, Investigator, or Karyopharm. Patients who have objective disease progression but have evidence of overall clinical benefit may, at the request of the treating physician, continue treatment with study drugs after discussion with the Medical Monitor.
- Follow-up period: durability of response and survival phone call will be made to patient every 3 months up to one year after last dose of study treatment.

1.5. MODIFICATIONS TO THE STATISTICAL SECTION OF THE PROTOCOL

The current SAP is based on Protocol Version 2.0 dated 26 May 2021.

1.6. STATISTICAL MODIFICATIONS MADE IN THE STATISTICAL ANALYSIS PLAN

None.

2. GENERAL STATISTICAL METHODS AND DATA HANDLING

This statistical analysis plan (SAP) outlines the methods to be used in the analysis of clinical data in order to answer the primary and secondary study objectives. Populations for analysis, data handling rules, and statistical methods are provided. CCI [redacted]

2.1. GENERAL ANALYSIS METHODS

All summary statistics will be computed and displayed among the corresponding analysis population, and by each scheduled assessment time point whenever applicable. Summary statistics for continuous variables will minimally include n, median, mean, standard deviation, minimum, and maximum. For categorical variables, frequencies and percentages will be presented with the denominators for the percentages determined based on the analysis population used, unless otherwise specified. For time-to-event variables, the Kaplan-Meier method will be used for descriptive summaries. Graphical displays will be provided as appropriate.

2.2. MISSING DATA HANDLING

In general, missing baselines will not be imputed. The following approaches are default methods for missing data handling in summary tables.

- Categorical data at baseline will be summarized using counts (n) and percentages (%). Denominator will be the total number of people in a corresponding treatment arm, based on the population specified for the summary, unless otherwise specified. Missing data may be presented as a separate category.
- Continuous data: summaries will be based on observed data only.

2.2.1. Handling of Computation of Treatment Duration if Study Treatment End of Treatment Date is Missing

For the calculation of treatment duration, the date of the last dose of study treatment is equal to the date of last study treatment dosing reported on study treatment dosing form. If all the dosing dates are missing, then the duration is missing.

The last dose intake should be clearly identified on the eCRF dosing page and should not be approximated by the last returned package date.

2.2.2. Handling of Missing/Partial Dates for Adverse Events or Concomitant Medications

In general, the imputation should be conservative such that onset dates should be imputed to be as early as possible and resolution dates will be imputed to be as late as possible. Impute resolution date first and then impute onset date using imputed resolution date. However, for categorization purpose, if the partial AE onset date information does not indicate whether the AE started prior to treatment or after the treatment-emergent adverse event (TEAE) period, the AE will be classified as treatment-emergent.

These data imputations are for categorization purpose or calculation of AE duration, and will not be used in listings.

Refer to the Karyopharm Biostatistics and Statistical Programming Rule Book 2.0 for details on imputation methods.

2.2.3. Handling of Missing or Partial Birth Date for Calculation of Age

Refer to the Karyopharm Biostatistics and Statistical Programming Rule Book 2.0 for details on imputation methods.

2.2.4. Handling of Missing Assessment of Relationship of AEs to Study Treatment

If the assessment of the relationship to study treatment is missing, then the relationship to study treatment in the frequency tables is considered as related.

2.2.5. Handling of Missing Severity of AEs

If the severity is missing for one of the treatment-emergent occurrences of an AE, the maximal severity on the remaining occurrences will be considered. If the severity is missing for all the occurrences, a "missing" category will be added in the summary table.

2.3. STUDY TREATMENT DOSING DATE

Study treatment dosing date is the date on which a patient actually received study treatment (partial or complete), as recorded on the study drug exposure eCRF.

The date of first study treatment is defined as the earliest date of non-zero dose of study treatment.

The date of last study treatment is defined as the latest date of non-zero dose of study treatment.

2.4. OBSERVATION PERIOD

The observation period will be divided by the following:

- The pre-treatment period is defined as the time from the signed informed consent date up to the time before the start date of study treatment.
- The treatment period is defined as the time from the start date of study treatment up to the last day of study treatment+30 days inclusive, or the day before initiation of a new anti-neoplastic treatment, whichever occurs first.
- The post-treatment period is defined as the time beyond the treatment period.

2.5. STUDY DAY CALCULATION

Study Day 1 is the date of first study treatment. The day before Day 1 is considered Day -1; there is no Day 0.

A patient is considered as treated in a cycle if the patient received any non-zero dose of study treatment in that cycle.

Study day for a given assessment is defined as

- the assessment date – the date of first study treatment + 1 if the assessment date is on or after Day 1, or
- the assessment date – the date of first study treatment if the assessment date is before Day 1.

2.6. BASELINE MEASUREMENT

For treatment period, the baseline value is defined as the latest value prior to the first dose of study treatment.

In the case an assessment performed on the same date as the first dose, but it is impossible to determine the evaluation time relative to the time of taking the first dose, the evaluation time will be assumed to be following the protocol-defined schedule.

2.7. SUBGROUPS

No subgroup analysis is planned due to the small sample size.

2.8. POOLING OF CENTERS FOR STATISTICAL ANALYSES

All participating centers in the study will be pooled together for analysis.

2.9. COMPUTING AND CODING STANDARDS

Activities will be performed using the following tools:

Table 2-1 Coding Standards

Table, listing, and figure production	SAS Version 9.4 or higher
Coding	
AEs	MedDRA Version 24.1 or higher
Medical Histories	MedDRA Version 24.1 or higher
Prior and Concomitant Medications	WHODrug-Global-B3/202109
Grading	
AEs	CTCAE Version 5.0 or higher

3. PATIENT INFORMATION

3.1. DISPOSITION OF PATIENTS AND ANALYSIS POPULATIONS

Patient disposition will be summarized in each of the following categories:

- Patients who were randomized
- Patients who were randomized and received at least one dose of the study treatment (partial or complete)
- End of treatment:
    - Patients who discontinued treatment and primary reason for discontinuation
- Survival follow-up status
    - Patients in survival follow-up
    - Patients who died during survival follow-up
- End of study
    - Patients who discontinued from study and primary reason for study discontinuation

3.1.1. Intent-to-Treat (ITT) Population

Intent-to-Treat Population (ITT): All patients randomized to study treatment. Patients will be analyzed in the treatment arm to which they were randomized.

3.1.2. Safety Population

All patients who have been assigned to study treatment and who have received ≥1 dose of study drug. Patients will be analyzed according to the study treatment received.

3.2. DEMOGRAPHICS, MEDICAL HISTORY, AND BASELINE CHARACTERISTICS

In general, the baseline value is defined as latest value prior to the first dose of study treatment. Demographics, medical history and baseline characteristics will generally be summarized among ITT and safety populations, unless otherwise specified. P-values on demographic, medical history and baseline characteristic data will not be calculated.

3.2.1. Demographic Data

Demographic variables include sex, race, ethnicity, and age at study entry.

3.2.2. Baseline Characteristics

Summary statistics including the number and percentage of patients will be presented for the following variables:

- Baseline height (cm)/ weight (kg)/ body surface area (m2)/ BMI (kg/m2)
- Baseline ECOG performance status

3.2.3. Prior Antineoplastic Therapy

Prior antineoplastic therapy will be summarized with the following variables:

- Number of prior regimens of antineoplastic therapy
- Best response to prior regimens of antineoplastic therapy
- Days since discontinuation of most recent prior antineoplastic therapy the start of study treatment, which will be calculated as the date of first study treatment – stop date of most recent antineoplastic therapy+1
- Days since most recent disease progression to the start of study treatment

The detailed history of prior systemic therapy including start and end dates of the medication, best response, progression during or after therapy, as well as discontinuations due to, toxicity and/or intolerability may also be provided in a data listing.

3.2.4. Medical/surgical History

Medical history will be summarized in the ITT population by system organ class (SOC) and preferred term (PT) using the number and percentage of patients who have at least one occurrence of a SOC and PT. The summary will be sorted by alphabetic order in SOC, and further by decreasing frequency of PT within each SOC. When more than one PT has the same frequency, the order of presentation will be alphabetical in PTs.

3.2.5. Disease History

Summary statistics including the number and percentage of patients will be presented for the disease history at initial diagnosis and/or screening

3.3. CONCOMITANT MEDICATIONS AND PROCEDURES

Concomitant medication consists of any prescription or over-the-counter preparation, including vitamins, dietary supplements, over-the-counter medications, and oral herbal preparations taken during the study, as well as changes in medication. Patients may continue their baseline medication(s). Concomitant medications include any medications used to treat symptoms, concomitant diseases such as diabetes, hypertension, etc., AEs and intercurrent illnesses that are medically necessary as part of standard care. All concomitant medication(s) must be reported on the eCRF. Any diagnostic, therapeutic, or surgical procedure performed during the study period should be recorded, including the dates, description of the procedure(s), and any clinical findings, if applicable. Concomitant medication will generally be summarized among ITT and safety populations, unless otherwise specified.

All medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO DDE, WHODrug-Global-B3/202109).

Prior medications are any treatments received by the patient prior to the first dose of study treatment. Prior medications can be discontinued before first dose of study treatment or can be ongoing during treatment period.

Concomitant medications are any treatments received by the patient concomitantly with study treatment, from first dose of study treatment to last dose of study treatment + 30 days.

Concomitant medications will be summarized according to the WHO DDE by the ATC level 2 (therapeutic level), level 4 (generic level) and standard name. A patient taking the same drug multiple times will only be counted once.

Note that a medication can be classified as both a prior medication and a concomitant medication.

The use of prior and concomitant medications and procedures may also be provided in a data listing.

3.4. EXTENT OF STUDY TREATMENT EXPOSURE AND COMPLIANCE

Study treatment is considered taken when patient actually received any study drug, partial or complete. Extent of exposure and compliance will generally be summarized among ITT and safety populations, unless otherwise specified.

The extent of exposure for the study treatment will be assessed using the following variable:

- Duration of study treatment exposure

The following will be presented separately for selinexor, pembrolizumab, trifluridine, and tipiracil:

- Duration of exposure
- Total dose received
- Average dose received per week
- Number and percentage of patients with dose reduction
- Number and percentage of patients with dose interruption
- Number and percentage of patients with missed dose

Duration of exposure is defined as the date of last dose - date of first dose + 1.

3.4.1. Treatment Compliance

Study treatment compliance will be summarized descriptively as a quantitative variable, calculated as

$$\frac{\text{number of study treatment doses taken}}{\text{number of study treatment doses prescribed}} \times 100\%.$$

Note that the number of scheduled study treatment doses does not include doses missed due to treatment interruption or other reasons not related to patient choice.

Treatment compliance will also be presented separately for selinexor as

$$\frac{\text{number of actual doses taken}}{\text{number of doses scheduled}} \times 100.$$

Similarly, the number of scheduled doses does not include doses missed due to treatment interruption or other reasons not related to patient choice.

4. EFFICACY

Response assessment will be determined per RECIST 1.1 for all arms at the time points specified by the investigator. All efficacy analyses will be performed on the ITT Population.

4.1. EFFICACY ENDPOINTS

4.1.1. Overall Response Rate (ORR)

ORR is defined as the proportion of patients who have a response of partial response (PR) or complete response (CR) as assessed by RECIST 1.1 before disease progression or initiating a new antineoplastic treatment. ORR can be computed based on best overall response (BOR) of each patient. BOR is only censored by disease progression, new antineoplastic treatment event, database cut.

For descriptive purposes, a two-sided exact 95% CI of ORR will also be presented. The number and percentage of patients in the following response categories will also be presented, along with exact 95% CIs: CR, PR, SD, and NE.

4.1.2. Disease control rate (DCR)

DCR is defined as the proportion of patients who have best response of PR or better, or at least 12 continuous weeks of SD before disease progression or initiating a new antineoplastic treatment. For descriptive purposes, a two-sided exact 95% CI will also be presented.

4.1.3. Progression-free Survival (PFS)

PFS is defined as the time from the randomization date until the date of first PD determined by PI per RECIST 1.1, or death due to any cause, whichever occurs first. The outcome and censoring definitions are provided in Table 4-1. The number and percentage of censored patients will be reported. The 25^{th}, 50^{th} (median), and 75^{th} percentiles for PFS and associated 95% CIs will be estimated based on the KM method.

4.1.4. Duration of Response (DOR)

DOR is defined for patients with PR or CR as the duration from the date of first PR or better to the date of first PD or death due to any cause, whichever occurs first. Details on the outcome and censoring definitions used for DOR are provided in Table 4-1.

The number and percentage of censored patients will be reported. The 25^{th}, 50^{th} (median), and 75^{th} percentiles for DOR and associated 95% CIs will be estimated based on the KM method.

4.1.5. Overall Survival (OS)

OS is defined as time since the randomization date until death due to any cause. If death event did not occur during the follow-up period, the patient is censored at the date of discontinuation from the study, or date of last participating visit (e.g., a telephone contact with patient status being alive) on or before database cut-off date, whichever occurs first.

Table 4-1 PFS or DOR (responders only) outcome and censoring definition

Situation	Date of event or censoring	Outcome
No adequate post-baseline disease status assessment unless death occurs prior to first post-baseline assessment	Date of first study treatment	Censored
Death due to any reason before PD	Date of death	Event
PD	Date of PD	Event
No PD or death due to any reason on or before a. database cut, b. withdrawal of informed consent, c. lost to follow-up, d. start of new antineoplastic treatment, whichever occurs first	Date of last adequate disease assessment on or prior to the earliest occurrence of the events (a. – d.) listed in the left column	Censored
No PD or death due to any reason	Date of last adequate disease assessment prior to the gap	Censored

4.2. STATISTICAL METHODS FOR EFFICACY ENDPOINTS

Binary endpoints of ORR and DCR will be calculated by point estimate with a 95% confidence interval (CI) using the exact method.

The analysis of time-to-event endpoints (PFS, OS, DOR) will be based on Kaplan-Meier method for estimation of summary statistics and will include the median event times and associated 95% CIs, as well as the number and percentage of censored patients. In addition, Cox proportional hazards regression models will be used to estimate a HR for the risk of progression in the selinexor only or selinexor and pembrolizumab arm versus the SOC control arm, and the selinexor and pembrolizumab arm versus selinexor only arm comparisons.

5. SAFETY

Safety analyses will use safety population evaluated by means of AE reports. The analyses of the safety variables will be essentially descriptive, and no statistical testing is planned.

5.1. ADVERSE EVENTS

An AE is defined as any untoward medical occurrence in a patient receiving a pharmaceutical product regardless of a causal relationship with this treatment. An AE can therefore be any unfavorable sign and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a study treatment, whether or not related to the study treatment.

All AEs (including serious adverse events [SAEs]) will be coded to a preferred term (PT) and associated primary system organ class (SOC) using the MedDRA.

The severity of all AEs will be graded according to the NCI CTCAE Grading Scale, Version 5.0. An AE with a CTCAE grade of 3 or higher is considered a severe AE. The severity of the AE is different from the seriousness of the AE. For AEs not covered by CTCAE, the severity will be characterized as "mild," "moderate," "severe", "life-threatening" (corresponding to Grades 1 to 4) according to the following definitions:

- Mild events are usually transient and do not interfere with the patient's daily activities.
- Moderate events introduce a low level of inconvenience or concern to the patient and may interfere with daily activities.
- Severe events interrupt the patient's usual daily activities.
- Life-threatening.

5.1.1. Definitions of Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Treatment-Emergent Treatment-Related Adverse Events (TRAEs)

5.1.1.1. Treatment-Emergent Adverse Event (TEAE)

Treatment-emergent adverse events (TEAE) of study treatment are defined as any event that was not present prior to the initiation of any study treatment (selinexor and/or other drugs) or any event already present that worsens in either intensity or frequency following exposure to study treatment, from the first dose of study treatment to 30 days after the last dose of study treatment inclusive, or the day before the start of a new antineoplastic treatment, whichever occurs first. Additionally, any AEs that occurred 30 days after the last dose of study treatment or after the start of a new antineoplastic treatment will also be considered as TEAE, if assessed by the Investigator as related to any drug of the study treatment.

5.1.1.2. Serious Adverse Event (SAE)

An SAE is any untoward medical occurrence, at any dose, that:

- Results in death

- Is life-threatening (i.e., an event in which the patient was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Results in a congenital anomaly/birth defect

Important medical events that may not result in death, are not life-threatening, or do not require hospitalization may be considered SAEs when, based on appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. SAE needs to be clearly documented on the AE form. SAEs that occur at any time between the signing of the ICF up to the first dose of study treatment, must be reported (in addition to SAEs that occur after the first dose of study treatment).

5.1.1.3. Treatment-emergent Treatment-Related Adverse Events (TRAEs)

A TRAE is any TEAE that is related to any study treatment.

5.1.2. Analysis Methods

The primary focus of AE reporting will be on TEAEs.

If an AE date/time of onset (occurrence or worsening) is incomplete, an imputation algorithm will be used to determine the AE as treatment-emergent. The algorithm for imputing date/time of onset will be conservative and will classify an AE as treatment-emergent unless there is definitive information to determine it is not treatment emergent. Details on classification of AEs with missing or partial onset dates are provided in Section 2.2.2.

AE summaries will include number (n) and percentage (%) of patients who have experienced an AE. The denominator for computation of percentages is the number of patients in the corresponding treatment arm. Multiple occurrences of the same event in the same patient will be counted only once in the tables.

Unless otherwise specified, sorting order will follow the alphabetic order in SOC, and further by decreasing frequency of PTs within each SOC. When more than one PT has same number of events, the order of presentation will be alphabetical in PTs.

The summary of AEs by causality will generally include the following categories of causality.

- Related to selinexor or pembrolizumab or trifluridine or tipiracil
- Related to selinexor only
- Related to pembrolizumab only
- Related to trifluridine only
- Related to tipiracil only
- Not related to selinexor or pembrolizumab or trifluridine or tipiracil

5.1.3. Analysis of TEAE

An TEAE overview summary table will be provided, which will include the number of patients with at least one of the adverse events:

- TEAEs
- Grade 3/4 TEAEs
- Serious TEAEs
- TEAEs leading to dose modifications of study treatment
- TEAEs leading to dose reduction of study treatment
- TEAEs leading to dose interruption of study treatment
- TEAEs leading to study treatment discontinuation
- TEAEs leading to death
- TRAE
- Serious TRAEs
- TRAEs leading to dose modifications of study treatment
- TRAEs leading to dose reduction of study treatment
- TRAEs leading to dose interruption of study treatment
- TRAEs leading to study treatment discontinuation
- TRAEs leading to death

TEAEs will be summarized by primary SOC and PT and will include the following categories:

- All TEAEs
- All TEAEs, by causality
- All TEAEs, by maximum grade
- TEAEs leading to dose modifications of study treatment
- TEAEs leading to study treatment discontinuation

5.1.4. Analysis of SAE

Treatment-emergent SAEs will be summarized by primary SOC and PT and will include the following categories:

- All treatment-emergent SAEs
- All treatment-emergent SAEs, by causality
- Treatment-emergent SAEs leading to dose modifications of study treatment
- Treatment-emergent SAEs leading to study treatment discontinuation

5.2. DEATH

The following summaries on death events will be provided:

- An overview of all death events and primary cause of death
- TEAEs leading to death by primary SOC and PT
- Listing of all death events

6. REFERENCES

1. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargen, D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009; 45:228-47.

2. Karyopharm Biostatistics and Statistical Programming Rule Book, Karyopharm Therapeutics Inc., version 2.0

Document Approvals

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