## SPONSOR:

BioMed Valley Discoveries

## PROTOCOL NUMBER:

BVD-523-ABC

# STATISTICAL ANALYSIS PLAN

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| **Author:** | **David Manteigas** |
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# 1 Cover and signature pages

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| **Protocol Number:** | BVD-523-ABC |
| **Study Title:** | A Two-Part, Phase II, Multi-center Study of the ERK Inhibitor Ulixertinib (BVD-523) for Patients with Advanced Malignancies Harboring MEK or Atypical BRAF Alterations |
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**We, the undersigned, confirm that we have read, understood and agree to the content of this document and hereby authorise its approval.**

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# 2 Table of Contents

# 3 List of Abbreviations

| | |
|---|---|
| AE | Adverse Event |
| ATC | Anatomical Therapeutic Chemical Classification |
| BOR | Best Overall Response |
| BRAF | V-raf murine sarcoma viral oncogene homolog B1 |
| BVD | BioMed Valley Discoveries |
| CI | Confidence interval |
| CM | Concomitant medications |
| CR | Complete Response |
| CRA | Clinical Research Associates |
| CRC | Colorectal cancer |
| CRO | Clinical Research Organization |
| DBP | Diastolic blood pressure |
| DOR | Duration of response |
| EAS | Evaluable Analysis Set |
| EC | Ethics Committee |
| eCRF | Electronic Case Report Form |
| ERK | Extracellular signal-regulated kinase |
| FAS | Full Analysis Set |
| ICF | Informed consent form |
| ICH | International Conference on Harmonization |
| IRB | Institutional Review Boards |
| IxRS | Interactive Voice/Web Response System |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MEK | Mitogen-activated protein kinase/extracellular signal-related kinase |
| mRNA | Messenger ribonucleic acid |
| NCI CTCAE | National Cancer Institute Common Terminology Criteria for Adverse Events |
| ORR | Overall Response Rate |
| OS | Overall survival |
| PD | Pharmacodynamic |
| PDCF | Protocol Deviation Criteria Form |

| | |
|---|---|
| PFS | Progression Free Survival |
| PK | Pharmacokinetic |
| PP | Per-protocol analysis set |
| PR | Partial Response |
| PT | Preferred Term |
| SAE | Serious adverse event |
| SAP | Statistical analysis plan |
| SBP | Systolic blood pressure |
| SMC | Safety Monitoring Committee |
| SOC | System Organ Class |
| TEAE | Treatment Emergent Adverse Event |
| TFLs | Tables, listings and figures |
| WHO | World Health Organization |

# 4 Introduction

The purpose of this document is to describe the statistical methods, data derivations and data summaries to be employed in the analysis of the Phase II study titled "A Two-Part, Phase II, Multi-center Study of the ERK Inhibitor Ulixertinib (BVD-523) for Patients with Advanced Malignancies Harboring MEK or Atypical BRAF Alterations". This study, set up by BioMed Valley Discoveries, aims at evaluating the safety and clinical benefit of ulixertinib as measured by the overall response rate (ORR) in patients receiving ulixertinib that have advanced malignancies harboring a MEK or atypical BRAF alteration. The study has two parts, Part A, aiming at assessing the clinical benefit of ulixertinib, followed by Part B, in patients with selected tumor types. The study will also include an initial assessment of the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of ulixertinib in patients.

This statistical analysis plan (SAP) covers the final analysis for both Part A and Part B of the study. Given that Part B is dependent upon Part A results, this version of the SAP will focus mostly on Part A analysis and a new version will be prepared to further detail Part B analysis once Part A analysis is complete. The list of tables, figures and listings (TFLs) to be developed for each analysis, as well as the shells for each TFL, are described in a separate document.

The preparation of this SAP is based on study Protocol version 1.0 from 01JUN2021, the most up to date electronic Case Report Form (eCRF) version and on the International Conference on Harmonization (ICH) E3 and E9 Guidelines.

# 5 Study Objectives

The primary, secondary, and exploratory objectives along with the associated endpoints as per the study protocol are presented as follows:

### *Part A – Tumor Histology Agnostic*

**Primary Objective**

- To assess the clinical benefit of ulixertinib as measured by the overall response rate (ORR) in patients receiving ulixertinib that have advanced malignancies harboring a MEK or atypical BRAF alteration.

*Primary Endpoint*

- ORR will be defined as the percentage of patients achieving a Best Overall Response (BOR) of confirmed Complete Response (CR) and/or Partial Response (PR), according to RECIST 1.1.

**Secondary Objectives**

- To evaluate the safety profile of ulixertinib.
- To assess the duration of response (DOR).
- To assess the progression free survival (PFS) and overall survival (OS) over 18 months.
- To measure the blood levels of ulixertinib and selected metabolites.

*Secondary Endpoints*

- Safety profile, including term, incidence, severity, and duration of AEs, as per CTCAE v5.0.
- DOR according to RECIST 1.1.
- PFS time according to RECIST 1.1.
- OS time.
- Pharmacokinetic profile of ulixertinib (BVD-523) and selected metabolites.

**Exploratory Objectives**

- To evaluate the effects of ulixertinib on pharmacodynamic markers.

*Exploratory Endpoint*

- ctDNA, tissue biopsies, and/or blood to access biomarkers. Assays include, but are not limited to, phosphorylation of RSK from whole blood, RPPA to assess protein levels, e.g. DUSP 4/6, plus Nanostring and/or RNA-exome to assess mRNA expression in tissue pre- and post-ulixertinib treatment.

### *Part B – Tumor Histology Specific*

**Primary Objective**

- To assess PFS in patients receiving ulixertinib in defined tumor histologies (up to three histologies to be selected) compared to physician's choice of treatment. Patient's tumors must harbor a specified MEK or atypical BRAF alteration.

*Primary Endpoint*

- PFS will be defined as the time from first day of trial medication to disease progression according to RECIST 1.1, or death.

**Secondary Objectives**

- To evaluate the safety profile of ulixertinib.
- To assess OS over 18 months in patients receiving ulixertinib with a defined tumor histology and specified MEK or atypical BRAF alteration, compared to physician's choice of treatment.

- To determine the ORR and DOR in patients receiving ulixertinib with a defined tumor histology and a MEK or atypical BRAF alteration, according to RECIST 1.1, compared to physician's choice of treatment.

*Secondary Endpoints*

- Safety profile, including term, incidence, severity, and duration of AEs, as per CTCAE v5.0.
- OS time.
- ORR and DOR according to RECIST 1.1.

# 6 Study Design

## *6.1 STUDY DESIGN AND POPULATION*

This is a two-part, phase II, multicenter study of the ERK inhibitor ulixertinib (BVD-523) with an open-label, tumor histology agnostic part (Part A) and a tumor histology specific part (Part B).

***Part A: Tumor Histology Agnostic***

Part A of the study will be open label and enroll patients to one of six groups based on their tumor alteration:

- *Group 1:* Patients with tumors, other than colorectal cancer (CRC), having a BRAF alteration that results in an amino acid change at positions G469, L485, or L597.
- *Group 2:* Patients with tumors, other than CRC, having a defined Class 2 BRAF alteration.
- *Group 3:* Patients with tumors, other than CRC, having an atypical BRAF alteration (non V600) that is not specified in Group 1 or Group 2.
- *Group 4:* Patients with CRC having any atypical BRAF alteration.
- *Group 5:* Patients with tumors, other than CRC, harboring alterations in MEK1/2.
- *Group 6:* Patients with CRC harboring alterations in MEK1/2.

***Part B: Tumor Histology Specific***

Part B of the study will randomly enroll patients with one of up to three specified tumor histologies to receive either ulixertinib or the physician's choice of treatment in a 2:1 ratio. Tumors must harbor a specified MEK or atypical BRAF alteration. If a patient progresses on physician's choice of treatment, crossover to the ulixertinib arm is permitted.

An overview of the study design is presented in Figure 1 below.

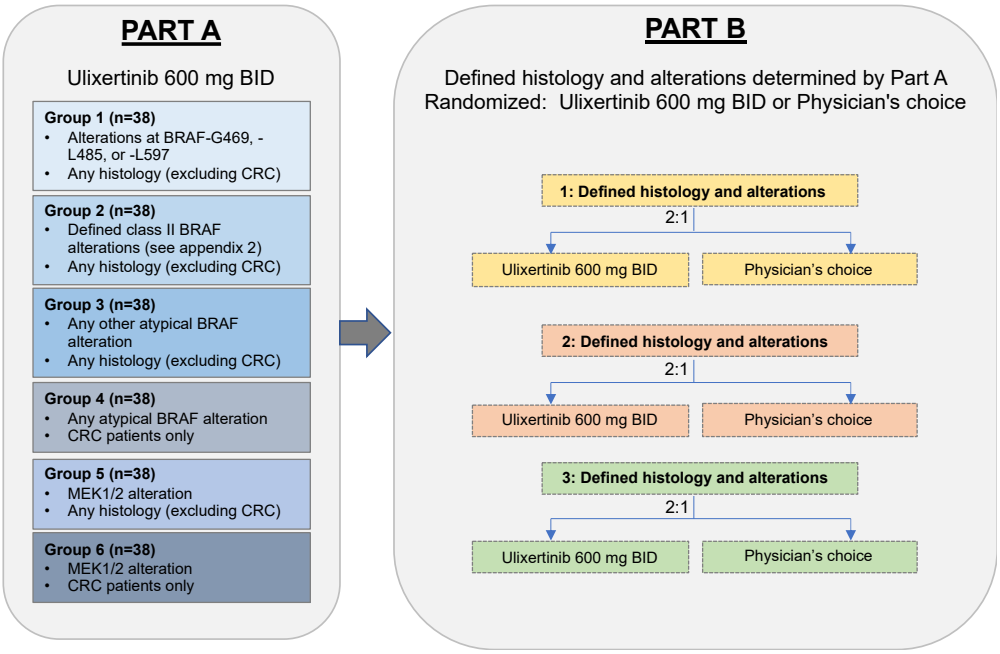


**Figure 1. Study Design**

Ongoing data from Part A will also be used to prioritize one or more tumor histologies that warrant study in Part B. The specific histologies and alterations to be included in Part B will be selected based on available data from Part A and discussion with the clinical investigators, the medical monitor, and the sponsor.

Part A of the study will enroll approximately 228 patients with 38 patients per group. Additional patients may be enrolled as appropriate. Part B of the study will enroll 80-100 patients per histology, with up to three histologies included, additional patients may also be enrolled.

The estimated duration of accrual is 21 months. The total duration of the study will be approximately 38 months.

Patients are considered to have completed the study if they have completed all phases of the study including the last visit or the last scheduled procedure.

Patients will continue on study therapy until documented disease progression, intolerable toxicity, study closure, or until other treatment discontinuation criteria is met. Patients who discontinue study therapy prior to disease progression, will continue to be followed for progression, survival or initiation of subsequent anticancer therapy for 18 months from the date of study therapy initiation. It is estimated that participants will be on study for up to 30 months.

Screen failures are defined as patients who consent to participate in the clinical trial but do not meet the criteria required for participation in the trial during the screening procedures. Patients who do not meet the inclusion criteria may be rescreened and will be assigned a new subject identification number.

### *6.2 STUDY TREATMENTS AND ASSESSMENTS*

Patients will receive 600 mg oral doses of ulixertinib, which is to be taken twice daily (b.i.d.) orally for 28 days, at 12-hour ± 2 hours intervals, approximately the same time each day with food and at least 8 ounces of water. Patients will be provided the study drug for a full cycle to self-administer at home.

Patients experiencing unacceptable toxicity will have their treatment interrupted until the toxicity returns to ≤ Grade 1 or pre-treatment baseline. Dose adjustments will be done in consultation with the investigators and medical monitor of the study. If a non-treatment related adverse event (AE) or toxicity-related dose delay lasts for > 21 days, treatment will be discontinued permanently, and the patient will be removed from study treatment.

### *6.3 RANDOMIZATION AND BLINDING*

Part A is designed as an open-label study. All patients in Part A will receive treatment with orally administered ulixertinib. Patients in Part B will receive either treatment with orally administered ulixertinib or the physician's choice of treatment in a 2:1 ratio. In Part B, if a patient progresses on the physician's choice of treatment then they may crossover to the ulixertinib arm.

Part B randomization will be performed as total enrollment rather than on a site basis.

Randomization/enrollment in both parts will be performed by using Interactive Voice/Web Response System (IxRS). In Part B, the IxRS will randomly assign the patient to one of the two treatment arms (ulixertinib or the physician's choice of treatment). In both parts, the IxRS will assign the patient a unique patient identification number. This patient identification number will then be reported on all eCRF pages and in any study documents.

### *6.4 SAMPLE SIZE JUSTIFICATION*

#### *Part A*

Approximately 38 patients will be recruited into each group in Part A.

With 34 patients in a group and assuming the true ORR is 40%, there is approximately 80% power to reject the null hypothesis that the true ORR is ≤ 20% in that group, with a 1-sided alpha of 5%. Assuming a 10% drop out rate, up to 38 patients will be recruited in each group.

#### *Part B*

Part B sample size estimation may be updated after Part A results are available.

Approximately 80-100 patients will be randomized, using a 2:1 ratio, for each histology group in Part B.

Using a 2-sided, log-rank test with a 5% alpha, and assuming a median PFS of 1.7 to 8.5 months (depending on histology) in the physician's choice arm and twice as long on the ulixertinib arm, approximately 80 to 100 patients will be required in each group to achieve 80% power to show a statistically significant difference between the arms. This also assumes that each group will take approximately 24 months to accrue, and the analysis is expected to be performed 18 months following the last patient accrued. The anticipated loss to follow-up is estimated to be 10%.

# 7 Statistical Considerations

## *7.1 STUDY TREATMENT*

The study drug is ulixertinib (BVD-523). The study treatment refers to treatment with ulixertinib (BVD-523). For Part B, the physician's choice treatment will be provided to patients in the comparator arm.

## *7.2 PLANNING OF ANALYSES*

This SAP covers final analysis for Part A and Part B, although the analysis for Part B will be further described once Part A results are available in an updated SAP version. The planned timing of analysis for Part A is 18 months after the last patient enrolled starts treatment. Since Part B depends on Part A results it is not possible to estimate by when Part B analysis will occur. The SAP will be updated after Part A results are available and the Protocol is amended.

Given that the study was early terminated during Part A, an abbreviated CSR focusing on safety will be prepared. Therefore not all Tables, Listings and Figures planned in SAP version 1 will be required. The Shells table of contents will have an additional column to indicate which outputs will be delivered for the final analysis of Part A.

### *7.3 STUDY AND ANALYSIS PERIODS*

Study periods are summarized in Table 1 below. Analysis periods will mirror these periods and are summarized in Table 2 below.

**Table 1. Study periods**

| Period | Visit | Planned days |
|---|---|---|
| Part A and Part B | | |
| SCREENING | Screening (up to 4 weeks before Baseline) | Day -28 to Day -1 |
| TREATMENT | Cycle 1 | Baseline<br>Day 8 ± 3<br>Day 15 ± 3 |
| | Cycle 2 | Day 29 ± 3<br>Day 36 ± 3<br>Day 43 ± 3 |
| | Cycle 3 – Cycle n | Day 57 ± 3 – Day n ± 3 |
| FOLLOW-UP | End of Treatment (EOT) Visit | ≤14 ± 3 days after last dose |
| | Safety Follow-Up | 30 ± 3 days after last dose |
| | Follow-Up | Every three months (± 7 days) until death, end of the study, or patient withdrawal of consent, whichever comes first. |

**Table 2. Analysis periods**

| Phase | Period | Definition |
|---|---|---|
| Part A and Part B | PRE-TREATMENT | From informed consent form (ICF) signature to the day before first dose of study treatment. |
| | ON-TREATMENT | From the day of first dose of study treatment to ≤14 ± 3 days after last dose of study treatment (date of EOT visit), or the earliest date of subsequent anti-cancer drug therapy – 1 day, whichever occurs first. |
| | FOLLOW-UP | From day ≤14 ± 3 after last dose of study treatment, or the earliest date of subsequent anti-cancer drug therapy, whichever occurs first, to end of study. End of study is date of completion / discontinuation from the study as collected in the CRF or the last recorded assessment in the database if the patient has not completed/discontinued the study at the time of the analysis. |

### *7.4 SOFTWARE*

The SAS Viya version 3.5 (or higher), will be used for all analysis, unless otherwise specified.

### *7.5 MISSING DATA HANDLING*

No imputation for missing data will be carried out other than to complete partial dates using standard imputation techniques as described below in Section 7.6.

### *7.6 PARTIAL DATE IMPUTATION*

Detailed rules for partial date imputation are described below.

A permanent new date variable should be created if there is a requirement to be used in determining flags (such as on-treatment flags), sort orders and other derived variables needed for a table, listing, or figure. Imputed date variable names will be defined in the derived dataset specifications.

Original (raw) date variables must not be overwritten. Imputed dates will not be displayed in the listings.

**General rules for Adverse events (AE) and prior and concomitant medications (CM)**

*In case of partial dates with missing day:*

For AE and CM, any partial start date during the month of first dosing will be imputed to be the date of first dose, taking the worst-case scenario.

For any AE and CM starting after the month of first dosing, the start date will be imputed to be the first day of the month.

For any AE and CM starting before the month of first dosing, the start date will be imputed to be the last day of the month.

Partial AE and CM end dates will be imputed to be the last day of the month or at the date of study discontinuation/completion, whichever occurs first.

*In case of partial dates with missing day and missing month:*

For AE and CM, any partial start date during the year of first dosing will be imputed to be the date of first dose, taking the worst-case scenario.

For any AE and CM starting after the year of first dosing, the start date will be imputed to be the first day of the year (i.e. 01 January).

For any AE and CM started before the year of first dosing, the start date will be imputed to be the last day of the year (i.e. 31 December).

Partial AE and CM end dates will be imputed to be the last day of year (i.e. 31 December) or at the date of study discontinuation/completion, whichever occurs first.

Some examples are given below (DDMMMYYYY).

In most cases, start dates are imputed as first day of the month or first of January.

**Table 3: Examples of missing dates imputation**

| Data Type | Start Date | Imputed Start Date | First Dose date | End Date | Imputed End Date |
|---|---|---|---|---|---|
| Adverse Event, Prior/Concomitant Meds | JAN2017 | 31JAN2017 | 11NOV2017 | MAR2017 | 31MAR2017 |
| Adverse Event, Prior/Concomitant Meds | MAR2017 | 01MAR2017 | 27JAN2017 | MAR2017 | 31MAR2017 |
| Adverse Event, Prior/Concomitant Meds | 2017 | 27JAN2017 | 27JAN2017 | 2017 | 16MAR2017£ |
| Adverse Event, Prior/Concomitant Meds | MAR2017 | 01MAR2017 | 27JAN2017 | MAR2017 | 01MAR2017* |
| Adverse Event, Prior/Concomitant Meds | JAN2017 | 31JAN2017 | 27FEB2017 | 2017 | 31DEC2017 |

£ Patient discontinued on 16MAR2017; * Patient discontinued on 01MAR2017.

**Rules for other partial dates**

Partial dates are not expected for death. However, should a partial date be present for death, the date will be imputed to be the day after the last visit/assessment date when the patient was known to be alive, if there is at least one visit/assessment during the month of the corresponding partial death date. If there is no visit/assessment performed during the month of the corresponding partial death date, then the partial death date would be imputed as the first day of the month. A similar approach will be followed for partial date for death in which only year is known.

If partial date is present for dates related to disease history, the same rules as for AE and CM will be applied.

### *7.7 VISIT WINDOWING*

Planned assessments will not be re-assigned to any planned visits using statistical programming based on assessment date. All the data will be analysed according to the planned visit as collected in the eCRF. Data obtained at unscheduled and repeat assessments will be considered for the derivation of baseline, worst on-treatment result for safety analyses (clinical safety laboratory evaluation, other safety data), and time to event analyses.

## *7.8 REPORTING GUIDELINES*

**Visit labels**

The visit labels displayed in Table 4 will be used to display results in the TFLs. Following Cycle 2, any subsequent Cycle will consider Day 1 as start of Cycle and not the days since first study dose as for Cycle 2.

**Table 4. Visit Labels**

| Period | Visit | TFLs Label |
|---|---|---|
| Part A and Part B | | |
| Screening: Day -28 to Day -1 | Screening Day -28 to Day -1 | Screening |
| Cycle 1 | Cycle 1 Day 1 | Baseline |
| | Cycle 1 Day 8 | C1D8 |
| | Cycle 1 Day 15 | C1D15 |
| Cycle 2 | Cycle 2 Day 29 | C2D29 |
| | Cycle 2 Day 36 | C2D36 |
| | Cycle 2 Day 43 | C2D43 |
| Cycle 3 | Cycle 3 Day 1 | C3D1 |
| … | … | … |
| Cycle n | Cycle n Day 1 | CnD1 |
| End of Treatment: ≤14 ± 3 days after last dose of study treatment. | End of Treatment Visit | EOT |
| Safety Follow-Up: 30 ± 3 days after last dose of study treatment. | Safety Follow-Up | SFU |
| Follow-Up: every three months (± 7 days) until death, end of the study, or patient withdrawal of consent, whichever comes first. | Follow-Up | FUn |

**Summaries of baseline and change from baseline**

Baseline and change from baseline will be calculated for all assessments, including additional assessments (if applicable), as follows:

- Baseline is defined as the last available assessment prior to first dose of study treatment, including additional assessments (where applicable). Assessments that occurred on the same day as first dose, when time of assessment is not available, will be assumed to be prior to first dose (unless the assessment is planned after first dose in the protocol).
- Change from baseline will be calculated as the difference between the post-baseline assessment value and the baseline value.

Whenever applicable, percent change from baseline will be calculated as the difference between the post-baseline assessment value and baseline value divided by the baseline value multiplied by 100.

**Unscheduled visit / Repeat assessments**

Data obtained at unscheduled and repeat assessments will be considered for the derivation of baseline, worst on-treatment result for safety analyses (clinical safety laboratory evaluation, other safety data), and time to event analyses.

All other data from unscheduled or repeat assessments will not be included in summaries and will only be presented in data listings, if not otherwise specified.

**N**

N will be the number of patients in the specified population and group.

**Summary presentation**

For Part A all outputs will be presented by molecular alteration group as defined in SAP section 6.1 and overall if not otherwise specified. For Part B, all outputs will be presented by the selected histology groups, physicians choice of treatment (pooling all treatments under just one group) and overall.

**Continuous data**

Continuous data will be summarized using number of patients (n), mean, standard deviation, median, first and third quartiles (Q1 and Q3), minimum value, and maximum value.

**Categorical data**

Categorical data will be summarized using n and percentage.

- All categories will be presented, even if no patients are counted in a particular category, unless otherwise stated.
- A Missing category will be displayed in all tables for categories where at least one missing value exists, unless otherwise specified.
- Counts of zero in any category will be presented without percentage.
- All summary percentages will be calculated using N, unless otherwise stated in a footnote.
- For AEs, medical history, prior and concomitant medications, the counts are based on single counts of patients with multiple events/treatments under the same category, while the percentages are calculated using N. Counts will be displayed by descending order of frequency for the overall group by dictionary hierarchy.

**Precision of summary statistics**

- Integer – Sample size (n, N) and number of missing data (if displayed).
- One additional decimal place than reported/collected – Mean, median, other percentile, confidence interval.
- Two additional decimal places than reported/collected – Standard deviation.
- Same number of decimal places as reported/collected – Minimum, maximum.
- Percentages – One decimal place.

**Study day**

Study day will be calculated as (assessment date – date of first study treatment dose) for pre-baseline assessments and [(assessment date – date of first study treatment dose) + 1] for post-baseline assessments, i.e. there will be no study day 0 and study day 1 will correspond to the first study treatment dose.

**Ordering**

Data will be presented in listings in order of group, patient ID, visit, assessment date/time, and assessment type/parameters chronological order unless otherwise specified. In case of clinical laboratory results, the listings will be presented in order of group, patient ID, parameter, assessment date/time, visit.

**Date format**

Dates will be presented in format DDMMMYYYY.

**Dictionaries**

Latest version of Medical Dictionary for Regulatory Activities (MedDRA) will be used for the relevant outputs.

Latest version of World Health Organization (WHO) Drug Global B3 will be used for the relevant outputs.

NCI-CTCAE v5.0 will be used for the relevant outputs.

The version will be documented in the footnote of the corresponding TFLs.

**File naming**

Each TFL output file will be named with a t, l, or f added before the TFL number to denote the output type and then according to its table numbering in the following way: Table 14.2-1.1 would be t14_2_1_1, Table 14.2-11 would be t14_2_11, Listing 16.2.7-1.1 would be l16_2_7_1_1, and Figure 14.2-2.1 would be f14_2_2_1.

**Reporting guidelines**

- Page Orientation: Landscape.
- Tables and listings: will be created in .rtf.
- Figures: will be generated directly in .rtf.
- Font: Courier New font with minimum of 8-point font size.
- Margins: Left: 3.8 cm, Right: 2 cm, Top: 3 cm, Bottom: 2 cm, on letter paper.
- Columns header will be left aligned for listings.

# 8 Analysis Sets

**All Patients Analysis Set**

All Patients Set will include all patients who were enrolled (signed informed consent) regardless of whether they received the study drug or not.

**Full Analysis Set**

The full analysis set (FAS) will consist of all patients who received at least one dose of study drug. This analysis set will be used for all efficacy analyses.

For Part B, analyses performed on the FAS will allocate patients' treatment group as randomized.

**Safety Analysis Set**

The safety analysis set will consist of all patients who received at least one dose of study drug. This analysis set will be used for all safety analyses.

For Part B, analyses performed on the safety population will allocate patients' treatment group as actually received.

**Per Protocol Analysis Set**

The per-protocol analysis set (PP) will consist of all patients of the FAS who completed the study without any important protocol deviations. Prior to any analysis, all patients with important protocol deviations will be reviewed and a decision can be made to include a patient in PP even when there is at least one important protocol deviation. Those cases, if any, will be properly documented in the study report.

**Evaluable Analysis Set**

The Evaluable Analysis Set (EAS) will consist of patients from FAS who had the first efficacy evaluation on Study Day 29±3. Prior to any analysis, all patients data will be reviewed and additional criteria for exclusion from EAS may be added (e.g. occurrence of one or more important protocol deviations). Those cases, if any, will be properly documented in the study report.

For Part A the Full Analysis Set and the Safety Full Analysis Set will be the same. Given that the study was early terminated and an abbreviated CSR focusing mostly on safety data will be prepared, EAS and PP will not be used in any analysis.

# 9 Methods of Analyses and Presentations

## *9.1 PATIENT DISPOSITION*

The patient disposition data will be presented by group and overall, for both Part A and Part B on the All Patients Analysis Set. The number and percentage of patients belonging to the following disposition modalities will be presented along with the reason for discontinuation: patients enrolled, patients eligible for inclusion in the study, patients completed/discontinued screening, patients completed/discontinued treatment, patients completed/discontinued study.

The number and percentage of patients in each analysis set will also be presented.

A consort diagram with disposition information will also be provided.

In addition, information on analysis sets, study completion and discontinuation, informed consent and failed inclusion and exclusion criteria will be listed.

For Part B, a listing of randomization will be presented.

## *9.2 PROTOCOL DEVIATIONS AND/OR VIOLATIONS*

ICH E3 Q&A R1 defines a protocol deviation as “any change, divergence, or departure from the study design or procedures defined in the protocol”, and important protocol deviations as “a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a patient's rights, safety, or well-being”. The non-compliance may be either on the part of the patient, the investigator, or the study site staff. The list of potential protocol deviations, including classification (Important/Non-important) for each protocol deviation, will be pre-defined in the Protocol Deviation Criteria Form (PDCF).

Protocol deviations identified during the trial by the Clinical Research Associates (CRAs), Medical Monitors, or Data Managers will be tracked throughout the study using a protocol deviation tracker and classified as Important/Non-important. All protocol deviations will be read into SAS® prior to reporting.

Prior to data lock for the primary and final analyses, a review classification meeting will be held to review protocol deviations and classifications, and to agree on the final analysis sets.

Important protocol deviations will be summarized (frequencies and percentages) by deviation category and summary term for both Part A and Part B on FAS.

A listing of all protocol deviations will be provided for all patients.

### *9.3 DEMOGRAPHIC AND BASELINE CHARACTERISTICS*

The following demographic and baseline characteristics will be summarized using descriptive statistics and presented by group and overall, for both Part A and Part B, on the FAS:

- Age at screening (years), as derived in the eCRF - continuous and categorical using EudraCT categorization (18-64, 65-84, ≥ 85)
- Gender
- Childbearing/Reproductive potential
- Ethnicity
- Race
- Height at screening (cm)
- Weight at screening (kg)
- BMI at screening (kg/m^2)
- ECOG performance status at screening
- Smoking history
- Gene (BRAF, MEK1/MAP2K1, MEK2/MAP2K2)
- Codon as reported in the eCRF
- Amino acid change as reported in the eCRF
- NGS Vendors

The following disease history characteristics will be summarized using descriptive statistics and presented by group and overall, for both Part A and Part B, on the FAS:

- Cancer Diagnosis (only reported diagnosis will be displayed, not all categories displayed in the CRF)
- Time since initial diagnosis (in months)
- Disease stage at initial diagnosis (from 1 to 4)
- Disease stage at enrollment (from 1 to 4)
- Method of diagnosis (cytological/histological)
- Prior Cancer Therapies/Regimens (Yes/No)
- Prior BRAF/MEK Inhibitor Therapies (Yes/No)
- Prior Radiation Therapies (Yes/No)

Time since initial diagnosis will be calculated as [(date of first dose of study treatment - date of diagnosis) / 30.4375].

In addition, listings of the above data will be produced for all patients.

A by-patient, detailed listing of smoking history will be also presented.

### *9.4 MEDICAL HISTORY AND CONCOMITANT DISEASES*

Medical history and concomitant diseases will be coded using MedDRA.

Medical histories are defined as events reported on the Medical History and Disease History eCRF pages, which started before the first study treatment date and were not ongoing at the first study treatment date.

Concomitant diseases are defined as diseases which started before the first study treatment date but were ongoing at the first study treatment date.

The number and percentage of patients with a medical history will be tabulated by group and overall, for both Part A and Part B, by system organ class (SOC) and preferred term (PT) on the Safety Analysis Set. A by-patient listing will be produced.

The number and percentage of patients with a concomitant disease will be tabulated by group and overall, for both Part A and Part B, for each SOC and PT using the FAS. A by-patient listing will be produced.

### *9.5 PRIOR THERAPIES*

The following summaries will be created by group and overall, for both Part A and Part B, on the FAS:

*Prior radiotherapy:*

- Received at least one prior radiotherapy
- Site of prior radiotherapies (only reported sites will be displayed, not all categories displayed in the eCRF)
- Most recent therapy received before study treatment start: duration of therapy (months) and site

For prior radiotherapy, duration in months will be calculated as [(end date of therapy – start date of therapy) + 1] / 30.4375.

*Prior Anti-Cancer Therapies:*

- Received at least one prior anti-cancer therapy
- Lines of prior anti-cancer therapies
- Most recent therapy received before study treatment start: regimen name, BOR, duration

of therapy (months), time since BOR, time since relapse/progression, and reason for discontinuation.

*Prior BRAF/MEK inhibitor therapies:*

- Received at least one prior BRAF/MEK inhibitor therapy
- Most recent therapy received before study treatment start: treatment name, BOR, duration of BOR, duration of therapy (months), and reason for discontinuation.

For prior anti-cancer therapies, duration in months will be calculated as [(end date of therapy - start date of therapy) + 1] / 30.4375.

Time since BOR (months) will be calculated as [(date of first study treatment - date of BOR)+1] / 30.4375.

Time since relapse/progression (months) will be calculated as [(date of first study treatment - date of Relapse/Progression) + 1] / 30.4375.

For prior BRAF/MEK inhibitor therapies, duration in months will be calculated as [(end date of therapy - start date of therapy) + 1] / 30.4375.

*Prior and Concomitant Medication:*

Medications other than the study treatment will be coded using the WHO Drug Global dictionary. The version of the dictionary will be provided in the corresponding TFLs footnotes.

Medications will be defined as follows:

- Prior Medication: any medications whose end date is before the first study treatment date.
- Concomitant Medication: any medications whose start or end date is either the same or after the first dose of study treatment and up to the end of the on-treatment period.
    - Any medication with a missing medication end date will be assumed to be concomitant medication.
    - Ongoing medications are considered as concomitant medications.

The number and percentage of patients with prior and concomitant medications will be tabulated by group and overall, for both Part A and Part B, by Anatomical Therapeutic Chemical Classification (ATC) and preferred term (PT) on the FAS. A by-patient listing will be produced for prior and concomitant medications as well as for all prior therapies.

*On treatment Radiation, Surgery and Medical Procedures, and Blood Transfusions:*

On treatment Radiation, Surgery and Medical Procedures, and Blood Transfusions will be listed on the FAS.

### *9.6 STUDY DRUG EXPOSURE AND/OR COMPLIANCE*

Duration on treatment and cumulative dose received will be calculated for ulixertinib as defined below.

**Part A**

- *Number of cycles received =*
  Number of cycles where the patient received at least one dose.

- *Duration of exposure (months) =*
  [(Date of last known treatment dosing with ulixertinib – date of initial dosing with ulixertinib) + 1] / 30.4375

- *Planned cumulative dose (mg) =*
  Number of cycles received x 28 x 2 x 600.

- *Actual cumulative dose received (mg) =*
  Sum of [(number of capsules dispensed – number of capsules returned) x 150].

- *Relative dose intensity =*
  100 x Actual dose intensity / Planned dose intensity, with:
  - Actual dose intensity (mg/day) = Actual cumulative dose received (mg) / Duration of exposure (days).
  - Planned dose intensity (mg/day) = Planned cumulative dose (mg) / Duration of exposure (days).

Summary statistics will be presented for the number of cycles received, duration of exposure, actual cumulative dose, and relative dose intensity, by group and overall for Part A on the FAS.

The number and percentage of patients having at least one dosing interruption or adjustment will be tabulated with the corresponding reason by group and overall for Part A on the FAS. A by-patient listing will be produced.

Part B study drug exposure and compliance will be further described in an updated SAP version once Part A results are available.

## *9.7 PHARMACOKINETIC/ PHARMACODYNAMIC ENDPOINTS AND ANALYSES*

### *9.7.1 Pharmacokinetic Data*

Blood samples will be collected when the patient is at steady state (patients who have received at least 5 days, or 10 consecutive doses, of investigational product) to measure ulixertinib and selected metabolites plasma concentrations. Plasma concentration will be listed and summarized by analyte and visit including the Geometric mean and Coefficient of Variation. All data will be listed but tables will only include data that was collected when ulixertinib was at steady state as required by protocol.

### *9.7.2 Pharmacodynamic Data*

Blood samples will be collected pre-dose and 4 hours +/- 10 minutes post-dose on cycle 1 day 1, and cycle 1 day 15 to measure phosphorylation of ERK1/2 target RSK (pRSK). Percent inhibition of pRSK compared to baseline will be listed and summarized.

## *9.8 EFFICACY DATA ENDPOINTS AND ANALYSES*

All efficacy analyses will be performed on the FAS and replicated on PP and EAS as supportive analysis for Part B. For Part A only FAS and EAS will be used for efficacy analysis.

All efficacy data will be presented by group and overall, for both Part A and Part B, unless otherwise specified in the specific section.

### *9.8.1 Overall Response Rate (ORR) / Best Overall Response (BOR)*

Tumor response will be assessed by the Investigator using RECIST 1.1 criteria[1].

The decision for body areas to be scanned will depend on the extent of disease. Tumor assessments must include all known or suspected disease sites. Imaging will be performed on the abdomen, chest, pelvis, and the site of the primary tumor if elsewhere. Tumor measurements based on physical examination will occur at baseline and on the first day of each treatment cycle.

Tumor assessments will be made by CT/MRI/Physical Exam prior to dose initiation, at the 1st protocol-specified tumor measurement evaluation at the beginning of Cycle 2 and then every 2 cycles, and at End of Treatment. Patients that discontinue study treatment for any reason other than disease progression, must continue to have disease assessments every 8 weeks (± 7 days) until disease progression or the initiation of subsequent anticancer therapy. The schedule of tumor assessments should be fixed according to the calendar, starting with cycle one day one, regardless of treatment delays or interruptions due to toxicity. The same imaging technique used to characterize each identified and reported lesion at baseline will be employed in the following tumor assessments.

Anatomical measurements (target lesions) will be documented during screening and each subsequent evaluation. Objective assessments will be performed during screening and before the first study drug dose of every other cycle, starting with cycle 2.

The table below provides a summary of the overall response status determination at each time point.

**Table 5. Evaluation of Overall Response**

| Target lesions | Non-target lesions | New lesions | Overall response |
|---|---|---|---|
| CR | CR (or no non-target lesions) | No | CR |
| No target lesion [a] | CR | No | CR |
| CR | NE [b] | No | PR |
| CR | Non-CR/non-PD | No | PR |
| PR | Non-PD and NE (or no non-target lesions) [b] | No | PR |
| SD | Non-PD and NE (or no non-target lesions) [b] | No | SD |
| Not all evaluated | Non-PD | No | NE |
| No target lesion [a] | Not all evaluated | No | NE |
| No target lesion [a] | Non-CR/non-PD | No | Non-CR/non-PD |
| PD | Any | Yes or No | PD |
| Any | PD | Yes or No | PD |
| Any | Any | Yes | PD |
| No target lesion [a] | Unequivocal PD | Yes or No | PD |
| No target lesion [a] | Any | Yes | PD |

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, and NE = not evaluable.
[a] Defined as no target lesion at baseline.
[b] Not evaluable is defined as when either no or only a subset of lesion measurements is made at an assessment.

The ORR is defined as the percentage of patients having a confirmed response of either CR or PR. ORR will be calculated with the 95% confidence intervals (CIs). The 95% CIs will be estimated using the Clopper-Pearson method.

For Part B, ORR will be compared between ulixertinib and physician's choice of treatment using a Chi square test or Fisher's exact test as applicable.

Complete and partial response must be confirmed by a repeat assessment performed at > or = 4 weeks after the criteria for response are first met. Date of confirmed CR/PR will be the date of the first CR/PR that qualifies for confirmation. Additionally, patients with no post-baseline efficacy measurement due to reasons accountable for disease progression, will be assessed as non-evaluable and will count in the denominator of the ORR.

BOR will be assessed based on the tumor response at different evaluation time points from baseline until the first documented disease progression for RECIST or the last response assessment if there is no document disease progression at the time of the analysis. The order used to determine BOR is CR>PR>SD>PD, ignoring visits with missing tumor assessments. For SD to qualify for BOR, the SD assessment should be at least 6 weeks after first ulixertinib dose. BOR

date in this case will be the date of the first SD/PR/CR documented after 6 weeks.

The following table, based on Table 3 from the RECIST 1.1 guidelines[1], summarizes the algorithm describing how confirmed response and BOR are determined from the overall tumor assessments.

**Table 6. Evaluation of Confirmed BOR**

| Case | Overall response first timepoint | Overall response subsequent timepoint | Confirmed response/BOR |
|---|---|---|---|
| 1 | CR | CR | CR (if assessments at least 28 days apart). (note: sequence of CR – NE – CR would be considered as confirmed CR) |
| 2 | CR | PR | SD, PD, or PR<br>• If CR truly met at first timepoint, any subsequent assessment of PR should make the disease PD at that point. That is, neither a PR nor SD may follow CR.<br>• Therefore, SD, if CR assessment >=6 weeks (42 days after date of first treatment), otherwise PD.<br>• However, BOR may be PR if subsequent scans suggest small lesions were still present at first assessment (in which case first assessment of CR should be changed to PR) |
| 3 | CR | SD | SD or PD<br>• SD, if CR or SD assessment >=6 weeks (42 days) after date of first treatment,<br>otherwise PD |
| 4 | CR | PD | SD or PD<br>• SD, if CR assessment >=6 weeks (42 days after date of first treatment),<br>otherwise PD |
| 5 | CR | NE | SD or NE<br>• SD, if CR assessment >=6 weeks (42 days after date of first treatment<br>otherwise NE |
| 6 | PR | CR | PR (if assessments at least 28 days apart). |
| 7 | PR | PR | PR (if assessments at least 28 days apart). (note: sequence of PR – NE – PR would be considered as confirmed PR)<br>Where there are cases of more than one SD assessment between two PR assessments, then this should be discussed. |
| 8 | PR | SD | SD |
| 9 | PR | PD | SD or PD<br>• SD, if PR assessment >=6 weeks (42 days after date of first treatment),<br>otherwise PD |
| 10 | PR | NE | SD or NE<br>• SD, if PR assessment >=6 weeks (42 days after date of first treatment),<br>otherwise NE |
| 11 | SD | SD, PR, CR | SD |
| 12 | SD | PD | SD or PD<br>• SD, if SD assessment >=6 weeks (42 days after date of first treatment),<br>otherwise PD |

| Case | Overall response first timepoint | Overall response subsequent timepoint | Confirmed response/BOR |
|---|---|---|---|
| 13 | SD | NE | SD or NE<br>• SD, if SD assessment >=6 weeks (42 days after date of first treatment),<br>otherwise NE |
| 14 | NE, - | SD | SD |
| 15 | CR, PR, SD | - | SD or NE<br>• SD, if assessment >=6 weeks (42 days after date of first treatment) and does not qualify for CR or PR,<br>otherwise NE. |
| 16 | PD | | PD. Ignore all assessments after initial overall response of PD. |
| 17 | NE | NE | NE<br>Where all assessments are Not evaluable |

For changes in target tumor size, spider and waterfall plots will be presented. For all response assessments, swimmer plots will be presented. Target and Non-Target Lesions response assessments and incidence of new lesions will be summarized by visit and listed. All response assessments will be listed.

### *9.8.2 Duration of Response (DOR)*

The duration of response (in months) is defined as the period from the date of initial confirmed PR or CR until the date of first radiographically documented progressive disease or death from any cause. Only patients with BOR of CR or PR (i.e. responders) will be included in the analysis of duration of response.

DOR = [(Date of first PD/death – Date of first recorded confirmed CR/PR) + 1] / 30.4375

Patients with no documented progression or death after CR or PR will be censored at the last available tumor assessment (last assessment that is CR, PR, or SD):

DOR = [(Date of last assessment – Date of first recorded CR/PR) + 1] / 30.4375

The analysis of DOR will be performed with a Kaplan-Meier method (product-limit estimates) and a summary of associated statistics will be presented including corresponding two-sided 95% CI. The CI for the median will be calculated according to Brookmeyer and Crowley and CI for the survival function estimates at Month 3, 6, 9, 12, and 18 will be derived using the log-log transformation (SAS PROC LIFETEST CONFTYPE=LOGLOG), only if there are sufficient data for responders. However, the final choice of timepoints may be updated dependent upon the data.

Part B, DOR will be compared between ulixertinib and physician's choice of treatment using a Log Rank test or other appropriate test if the proportional hazards assumption does not hold.

### *9.8.3 Progression-free Survival (PFS)*

The PFS (in months) is defined as the time from the first ulixertinib dose until the first radiographically documented progression of disease or death from any cause, whichever occurs first.

PFS = [(Date of first PD/death – Date of first study treatment) + 1] / 30.4375

Patients with no documented progression or death will be censored at the last available tumor assessment (last assessment that is CR, PR or SD):

PFS = [(Date of last assessment where patient is PD free – Date of first study treatment) + 1] / 30.4375

For patients with no post baseline tumor assessment a censored PFS at day 1 will be considered.

PFS = (Date of first study treatment – Date of first study treatment) + 1

The analysis of PFS will be performed with a Kaplan-Meier method (product-limit estimates) and a summary of associated statistics will be presented including corresponding two-sided 95% CI. The CI for the median will be calculated according to Brookmeyer and Crowley and CI for the survival function estimates at Month 3, 6, 9, 12, and 18 will be derived using the log-log transformation (SAS PROC LIFETEST CONFTYPE=LOGLOG). However, the final choice of timepoints may be updated dependent upon the data.

For Part B, for each histology, PFS curves will be compared between ulixertinib and physician's choice of treatment using Log Rank Test or other appropriate test if the proportional hazards assumption does not hold.

### *9.8.4 Overall Survival (OS)*

The OS (in months) is defined as the time from first treatment to death. Patients who did not die during the study will be censored at the last known alive date.

OS = [(Date of death – Date of first study treatment) + 1] / 30.4375

For censored patients:

OS = [(Last known alive date – Date of first study treatment) + 1] / 30.4375

The last known alive date will be determined among study treatment administrations, any visits where at least one assessment has been completed, or any follow-up assessment where the patient has been confirmed to be alive.

OS will be analyzed using the same Kaplan-Meier method used to analyze the DOR.

Part B, OS will be compared between ulixertinib and physician's choice of treatment using a Log Rank Test or other appropriate test if the proportional hazards assumption does not hold.

## *9.9 SAFETY DATA ENDPOINTS AND ANALYSES*

All safety analyses will be performed on the Safety Analysis Set using descriptive statistics.

All safety data will be presented by group and overall, for both Part A and Part B, unless otherwise specified in the specific section.

### *9.9.1 Adverse Events (AEs)*

The following definitions will be used:

- ***Treatment-emergent AEs (TEAEs):*** Treatment-emergent adverse event (TEAE) is defined as any AE that emerges during on-treatment period, after the 1st dose of the study agent.
- ***Related AEs:*** AEs suspected by the Investigator and/or Sponsor to have a relationship to study treatment (as recorded on the AE eCRF page, Causality = Related, Possibly Related, or missing).
- ***Serious Adverse Events (SAE):*** serious AEs (as recorded on the AE eCRF page, Does AE Meet the Definition of an SAE = Yes).
- ***AEs leading to treatment discontinuation:*** AEs leading to permanent discontinuation of study treatment (as recorded on the AE eCRF page, Action taken with study treatment = Drug withdrawn).
- ***AEs leading to dose reduction:*** AEs leading to dose reduction of study treatment (as recorded on the AE eCRF page, Action taken with study treatment = Dose Reduced).
- ***AEs leading to treatment interruption:*** AEs leading to treatment interruption of study treatment (as recorded on the AE eCRF page, Action taken with study treatment = Drug Interrupted).
- ***AEs leading to Death:*** adverse event leading to death (as recorded on the AE eCRF page, Results in death, or Outcome = Fatal, or Grade = 5).

An overview summary table will present the number and percentage of patients with a TEAE, including:

- TEAEs / TEAEs related to study treatment

- SAEs / SAEs related to study treatment
- TEAEs leading to treatment discontinuation / TEAEs related to study treatment leading to treatment discontinuation
- TEAEs leading to treatment discontinuation within 1 cycle / TEAEs related to study treatment leading to treatment discontinuation within 1 cycle
- TEAEs leading to treatment discontinuation following 1 cycle / TEAEs related to study treatment leading to treatment discontinuation following 1 cycle
- TEAEs leading to treatment interruption / TEAEs related to study treatment leading to treatment interruption
- TEAEs leading to treatment interruption within 1 cycle / TEAEs related to study treatment leading to treatment interruption within 1 cycle
- TEAEs leading to treatment interruption following 1 cycle / TEAEs related to study treatment leading to treatment interruption following 1 cycle
- TEAEs leading to dose reduction / TEAEs related to study treatment leading to dose reduction
- TEAEs leading to dose reduction within 1 cycle / TEAEs related to study treatment leading to dose reduction within cycle 1
- TEAEs leading to dose reduction following 1 cycle / TEAEs related to study treatment leading to dose reduction following cycle 1
- TEAEs leading to death / TEAEs related to study treatment leading to death
- TEAEs with grade ≥ 3 / TEAEs related to study treatment with grade ≥ 3

In addition, the following tables will be produced by SOC and PT:

- TEAEs / TEAEs related to study treatment
- Serious TEAEs / Serious TEAEs related to study treatment
- TEAEs and maximum CTCAE grade / TEAEs related to study treatment and maximum CTCAE grade
- TEAEs leading to treatment within/following discontinuation / TEAEs related to study treatment leading to treatment discontinuation
- TEAEs leading to treatment within/following interruption / TEAEs related to study treatment leading to treatment interruption
- TEAEs leading to dose reduction within/following cycle 1 / TEAEs related to study treatment leading to dose reduction within/following cycle 1
- TEAEs leading to death / TEAEs related to study treatment leading to death

The following tables will be produced by PT:

- TEAEs / TEAEs related to study treatment
- Serious TEAEs / Serious TEAEs related to study treatment

A patient with multiple occurrences of an AE will be counted only once in the AE category. SOCs will be sorted by descending order of frequency for the overall group, PTs will be sorted by descending order of frequency for the overall group within each SOC.

All deaths will be summarized and listed with the corresponding reasons, split by overall deaths, and deaths occurring after the first dose of ulixertinib.

The following listings will be provided:

- All AEs
- TEAEs
- SAEs
- Deaths

### *9.9.2 Clinical Safety Laboratory Evaluation*

All haematology, biochemistry, and urinalysis laboratory tests collected will be reported.

The numerical measurements and change from baseline of all haematology, biochemistry, and urinalysis laboratory tests will be summarized using descriptive summary statistics for each visit.

For laboratory tests covered by the NCI-CTCAE (version 5), laboratory data will be graded accordingly. 'Normal' will be assigned for all non-missing values not graded as 1 or higher. For laboratory tests where grades are not defined by NCI-CTCAE, results will be graded by the low/normal/high classifications based on laboratory normal ranges as collected in the CRF. Separate tables will be created for Gradable and Non-gradable laboratory values.

Haematology and biochemistry laboratory tests will be summarized by:

- Tables (Gradable and Non-gradable) to describe the worst on-treatment value by cycle.
- Shift tables (Gradable and Non-gradable) to compare baseline to the worst on-treatment value.

Listings of all laboratory data with values flagged to show the corresponding NCI-CTCAE grades and the classifications relative to the laboratory normal ranges will also be provided. Also results of serum pregnancy tests will be listed.

### *9.9.3 Other Safety data*

#### *9.9.3.1 Vital signs*

Vital signs include the following parameters: systolic blood pressure (SBP) (mmHg), diastolic blood pressure (DBP) (mmHg), pulse (beats/min), and temperature (°C).

The numerical measurements and change from baseline of all vital signs parameters will be summarized using descriptive summary statistics for each visit.

Shift tables of baseline to worst on-treatment result (low, normal, high, very high) will be presented.

**Table 7. Thresholds for classification of vital signs test results**

| Vital Sign | Criteria | Flag |
|---|---|---|
| Temperature | < 36.4°C | Low |
| | 36.4°C – 37.7°C | Normal |
| | > 37.7°C | High |
| Pulse | < 55 bpm | Low |
| | 55-100 bpm | Normal |
| | 101-150 bpm | High |
| | > 150 bpm | Very High |
| Systolic Blood Pressure | < 90 mmHg | Low |
| | 90-130 mmHg | Normal |
| | 131-160 mmHg | High |
| | ≥ 161 mmHg | Very High |
| Diastolic Blood Pressure | < 60 mmHg | Low |
| | 60-85 mmHg | Normal |
| | 86-100 mmHg | High |
| | ≥ 101 mmHg | Very High |

All Vital Signs will be Listed.

### *9.9.3.2 Electrocardiogram (ECG)*

ECG includes the following parameters: Heart Rate (beats/min), PR Interval (msec), QRS Duration (msec), RR Interval (msec), QT Interval (msec), and QT interval corrected for heart rate by the Fridericia's formula (QTcF) Interval (msec).

The numerical measurements at baseline of all ECG parameters will be summarized using descriptive summary statistics.

A listing of ECG evaluations will be created.

### *9.9.3.3 ECHO/MUGA*

ECHO/MUGA assessments at baseline will be summarized using descriptive summary statistics.

A listing of ECHO/MUGA evaluations will be created.

#### *9.9.3.4 Physical Examination*

Physical Examination includes the following parameters: HEENT, Thorax, Abdomen, Skin and Mucosae, Neurological, Extremities, Urogenital, General Appearance, Heart, Back, and Lymph Nodes.

All physical examination assessments at baseline will be summarized using descriptive summary statistics.

A listing of physical examination evaluations will be created.

#### *9.9.3.5 Ophthalmology exam*

A listing of ophthalmological examination assessments will be created.

#### *9.9.3.6 ECOG Performance status*

The number and percentages of patients will be tabulated for ECOG performance score categories at each visit.

A listing of all ECOG Performance status at all visits will be presented.

# 10 Interim Analyses

No interim analysis is planned. The outputs provided for the regular SMC data reviews are covered in a separate SAP.

# 11 Changes to Planned Analyses

No major changes to analyses planned in the protocol are expected.

A new analysis population was defined to further investigate efficacy. Although the SAP will be signed and finalized prior to the first study analysis, this new analysis population is for exploratory purposes only.

Demographic and baseline data was planned in the Protocol to be reported for all analysis populations. However, at least for Part A, this will only be reported on FAS. For Part B, this may

be revised and additional tables may be added for each analysis set.

# 12 Document History

| Date | Version | Modified by | Brief details of changes made to template |
|---|---|---|---|
| 20Dec2021 | 1.0 | David Manteigas | First SAP Version. |
| 09Jun2023 | 2.0 | David Manteigas | Updated version of the SAP to cover for the dry-run comments and to account for the required updates due to the study being early terminated. |

# 13 References

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

# 14 Appendices

## *14.1 Schedule of events*

**Table 14.1 Part A and B: Schedule of Activities**

| | | Cycle 1 Day 1 through 28 | | | Cycle 2 Day 29 through 56 | | | Cycle 3-X 28-day cycles, visit on 1st day of cycle | Post Treatment Period | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Visit** | **1 Screening** | **2 Baseline** | **3 Tx** | **4 Tx** | **5 Tx** | **6 Tx** | **7 Tx** | **8 -X Tx** | **End of Treatment (EOT) Visit** | **Safety Follow-Up[a]** | **Follow-Up[b]** |
| Visit Day | -28 to -1 | 1 ± 0 | 8 ± 3 | 15 ± 3 | 29 ± 3 | 36 ± 3 | 43 ± 3 | 57 ± 3 | ≤14 ± 3 days after last dose | 30 ± 3 days after last dose | |
| Informed consent | X | | | | | | | | | | |
| Inclusion/exclusion criteria | X | X | | | | | | | | | |
| Demography | X | | | | | | | | | | |
| Medical history[c] | X | X | X | X | X | X | X | X | X | | |
| Cancer history[d] | X | | | | | | | | | | X |
| Concomitant medications | X | X | X | X | X | X | X | X | X | | |
| Measure height | X | | | | | | | | | | |
| Measure weight | X | X | X | X | X | X | X | X | X | | |
| Vital signs | X | X | X | X | X | X | X | X | X | | |
| Physical examination[e] | X | | | | | | | | | | |
| ECOG | X | X | X | X | X | X | X | X | X | | |
| Ophthalmology exam[f] | X | | | | | | | | | | |
| Pregnancy test[g,h] | X | X[g] | | | X[h] | | | X[h] | X[h] | | |
| Clinical lab tests[i, j] | X | X[i] | X | X | X | X | X | X[j] | X | | |
| Electrocardiogram (ECG)[k] | X | | | | | | | | | | |
| ECHO cardiogram or MUGA | X | | | | | | | | | | |

**Table 14.1 Part A and B: Schedule of Activities**

| | | Cycle 1 Day 1 through 28 | | | Cycle 2 Day 29 through 56 | | | Cycle 3-X 28-day cycles, visit on 1st day of cycle | Post Treatment Period | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Visit** | **1 Screening** | **2 Baseline** | **3 Tx** | **4 Tx** | **5 Tx** | **6 Tx** | **7 Tx** | **8 -X Tx** | **End of Treatment (EOT) Visit** | **Safety Follow-Up[a]** | **Follow-Up[b]** |
| Assess current disease status[l] | X | | | | X | | | X | X | | X[m] |
| Study drug administration[n] | | X | | X | | | | | | | |
| Adverse events (AEs) | | X | X | X | X | X | X | X | X | X | |
| Obtain unused drug | | | X | X | X | X | X | X | X | | |
| Compliance by pill count | | | X | X | X | X | X | X | X | | |
| Study drug dispensed | | X | X | X | X | X | X | X | | | |
| Part A Only | | | | | | | | | | | |
| Tissue biopsy, if indicated[o,p] | X[o] | | | | X | | | | X[p] | | |
| Pharmacodynamic blood samples[q] | | X | | X | | | | | | | |
| ctDNA[r] | | X | | X | X | | | | X | | |
| Pharmacokinetic samples[s] | | | | X[s] | | | | | | | |
| Part B Only | | | | | | | | | | | |
| Randomization | X | | | | | | | | | | |

Table footnotes:

[a] Patients will return to the clinic or will be contacted for a safety follow-up assessment 30 days ± 3 days after the last dose of study drug was taken; or earlier if subsequent therapy for advanced malignancy is initiated prior to 30 days ± 3 days.

[b] Patients or their legally authorized representatives will be contacted every three months (± 7 days) until death, end of the study, or patient withdrawal of consent, whichever comes first. Survival and subsequent treatment status may be collected by public records, medical records, or by contacting the patient or their legally authorized representative by phone.

[c] Full medical history at screening, only review/update of history at subsequent visits.

[d] Oncologic history of the malignancy under study including prior regimens (duration of therapy, best response on therapy, date of discontinuation, and reason for discontinuation), surgery, and radiation therapy.

[e] Physical examinations should be symptom driven after the Screening Visit.

[f] Ophthalmological examinations will be performed by an ophthalmologist at screening, and whenever clinically indicated. In Part B, only patients in the ulixertinib arm need an ophthalmological exam. See section 10.1.5 for a full description of tests.

[g] ONLY if the screening serum pregnancy test was performed more than 1 day previously.

[h] After screening and baseline, if urine pregnancy test is positive, confirm with serum test.

[i] Visit 2 clinical lab samples should be collected pre-dose if not done during Screening Visit within 72 hours of start of treatment.

[j] Chemistry, hematology, and urinalysis. After Cycle 2, clinical labs to be performed prior to starting each new cycle or more frequently when clinically indicated at the investigator's discretion. See section 10.1.6 for a full description of test.

[k] Patients with a normal ECG in Cycle 1 do not need to have repeat ECGs in subsequent cycles. Patients should be supine for 5 minutes prior to the ECG.

[l] Tumor assessments will be made prior to dose initiation, at Visit 5, and then every 2 cycles. Patients who discontinue treatment for reasons other than progression will have assessments at the EOT visit (unless their previous assessment was performed within 28 days). The same imaging modality used for an individual patient (i.e. CT or MRI) at Screening should be maintained throughout the study.

[m] Patients that discontinue study treatment for any reason other than disease progression, must continue to have disease assessments every 8 weeks (± 7 days) until disease progression or the initiation of subsequent anticancer therapy.

[n] Study drug to be taken twice daily. The first dose should be taken in the clinic on days when PD sampling occurs i.e., Cycle 1/Visit 2 (Day 1) and Cycle 1/Visit 4 (Day 15), remaining doses on all other days to be self-administered by patient.

[o] Tissue biopsy for Part A only. If a patient has undergone a biopsy within ≤ 6 months and has not received any anticancer treatment since undergoing the biopsy, archival tissue from this biopsy may be used to fulfill screening tissue requirements.

[p] Tissue biopsy at final study visit/at progression is optional, but strongly encouraged to help elucidate mechanism of resistance.

[q] Collect pre-dose and 4 hour +/- 10 mins post-dose blood samples for PD.

[r] Collect plasma for ctDNA.

[s] Sample for PK should be collected pre-dose trough at steady state (patients who have received at least 5 days, or 10 consecutive doses, of study drug).

## *14.2 CTCAE v5.0 Grading for Laboratory Values*

**Table 8. Hematology Tests**

| Parameter | CTCAE Gradable† | SOC | CTCAE v5.0 Term |
|---|---|---|---|
| Hematocrit | No | | |
| Hemoglobin | Yes | Blood and lymphatic system disorders | Anemia |
| | | Investigations | Hemoglobin increased |
| Platelets | Yes | Investigations | Platelet count decreased |
| White blood cells | Yes | Investigations | White blood cell decreased |
| | | Blood and lymphatic system disorders | Leukocytosis |
| Red blood cell count | No | | |
| Neutrophils absolute | Yes | Investigations | Neutrophil count decreased |
| Lymphocytes absolute | Yes | Investigations | Lymphocyte count decreased |
| | | | Lymphocyte count increased |
| Monocytes absolute | No | | |
| Eosinophils absolute | No | | |
| Basophils absolute | No | | |

† For laboratory tests where grades are not defined by NCI-CTCAE, results will be graded by the low/normal/high classification based on laboratory normal ranges.

**Table 9. Serum Chemistry Tests**

| Parameter | CTCAE Gradable† | SOC | CTCAE v5.0 Term |
|---|---|---|---|
| Albumin | Yes | Metabolism and nutrition disorders | Hypoalbuminemia |
| Alkaline phosphatase | Yes | Investigations | Alkaline phosphatase increased |
| ALT | Yes | Investigations | Alanine aminotransferase increased |
| AST | Yes | Investigations | Aspartate aminotransferase increased |
| Blood urea nitrogen | No | | |
| Uric acid | No | | |
| Chloride | No | | |
| Cholesterol | Yes | Metabolism and nutrition disorders | Hypercholesterolemia<br>Hypocholesterolemia |
| Calcium | Yes | Metabolism and nutrition disorders | Hypocalcemia |
| | | | Hypocalcemia |
| Creatinine | Yes | Investigations | Creatinine increased |
| Lactate Dehydrogenase | Yes | Investigations | Lactate Dehydrogenase increased |
| Glucose | Yes | Metabolism and nutrition disorders | Hyperglycemia |
| | | | Hypoglycemia |
| Potassium | Yes | | Hyperkalemia |

| Parameter | CTCAE Gradable† | SOC | CTCAE v5.0 Term |
|---|---|---|---|
| | | Metabolism and nutrition disorders | Hypokalemia |
| Sodium | Yes | Metabolism and nutrition disorders | Hypernatremia |
| | | | Hyponatremia |
| Inorganic Phosphorus | No | | |
| Total bilirubin | Yes | Investigations | Blood bilirubin increased |
| Triglycerides | Yes | Metabolism and nutrition disorders | |
| Direct bilirubin | No | | |
| Total protein | No | | |

† For laboratory tests where grades are not defined by NCI-CTCAE, results will be graded by the low/normal/high classification based on laboratory normal ranges.

**Table 20. Urinalysis Tests**

| Parameter | CTCAE Gradable† | SOC | CTCAE v5.0 Term |
|---|---|---|---|
| Dipstick Evaluation Of Bilirubin | No | | |
| Dipstick Evaluation Of Blood | No | | |
| Dipstick Evaluation Of Glucose | No | | |
| Dipstick Evaluation Of Ketones | No | | |
| Dipstick Evaluation Of Leukocytes | No | | |
| Dipstick Evaluation Of Protein | No | | |
| Microscopic Examination Of Casts | No | | |
| Microscopic Examination Of Rbc | No | | |
| Microscopic Examination Of Wbc | No | | |
| pH | No | | |
| Specific Gravity | No | | |

† For laboratory tests where grades are not defined by NCI-CTCAE, results will be graded by the low/normal/high classification based on laboratory normal ranges.

## SPONSOR:

BioMed Valley Discoveries

## PROTOCOL NUMBER:

BVD-523-ABC

# STATISTICAL ANALYSIS PLAN
# TFL SHELLS

| | |
|---|---|
| **Author:** | **David Manteigas** |
| **Version:** | 2.0 |
| **Date:** | 01-Jun-2023 |

# 1 Cover and signature pages

| | |
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# 2 Document History

| Date | Version | Modified by | Brief details of changes made to template |
|---|---|---|---|
| 20Dec2021 | 1.0 | David Manteigas | First SAP version |
| 09Jun2023 | 2.0 | David Manteigas | Updated version to include dry-run comments and the required changes for the final analysis after the study was early terminated. |

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Y = Output that will be included in the final analysis

# 4 General programming notes

For Part A, all tables will be reported by molecular alteration group. For Part B, all tables will be reported by selected tumor histology group and treatment group. Tables for All Patients Set will include a column for Screen Failures.

An 'Overall' column will be included in all tables.

All tables marked as Part A & Part B in the TFLs list will be replicated, just changing the columns and page headers, as indicated in the table below. Shells will be created using Part A headers.

| **Table** | **Column headers** | | | | | | | **Phase in Page Header** |
|---|---|---|---|---|---|---|---|---|
| Part A | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Overall | Part A |
| | | | | | | | | |
| Part B | Group 1 | | Group 2 | | Comparator | | Overall | Part B |

The full-page header to be included for each delivery is indicated in the table below:

| **Delivery** | **Type** | **Page Header** |
|---|---|---|
| Dry run | Dry run | Dry-run – Part A/B |
| Final analysis | Draft | Draft – Part A/B |
| | Final | Final – Part A/B |

For the listings, all cases where 'Other' is present, please present the respective 'Other' specification.

All Listings will be sorted by Group and patient ID. A programming note will be added to each Listing when another variable is needed to make the sorting meaningful (e.g., assessment date).

Table 14.1-1.1 – Patient Disposition
All Patients Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Screen Failures N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|---|
| Patients enrolled [a] | XX | XX | XX | XX | XX | XX | XX | XX |
| Patients completed screening [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Discontinued from screening [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Primary reason for discontinuation [c] | | | | | | | | |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Pregnancy | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Screen Failure | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Study Terminated by Sponsor | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lost to Follow-up | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Technical Problems | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Physician Decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Withdrawal by Patient | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients rescreened [b] | | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients eligible for inclusion in the study [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients treated with study drug [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Patients who signed the informed consent.
[b] Percentages are calculated from the number of patients enrolled.
[c] Percentages are calculated from the number of patients who discontinued from screening.
[d] Percentages are calculated from the number of patients who were treated with study drug.
[e] Percentages are calculated from the number of patients who discontinued from treatment.
[f] Percentages are calculated from the number of patients who discontinued from study.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-1.1 - Patient Disposition
All Patients Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Screen Failures N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|---|
| Patients completed treatment [d] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Discontinued from treatment [d] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Primary reason for discontinuation [e] | | | | | | | | |
| Death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Pregnancy | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Withdrawal by Patient | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Protocol Violation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lost to Follow-up | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Physician Decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Study Terminated by Sponsor | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Patients who signed the informed consent.
[b] Percentages are calculated from the number of patients enrolled.
[c] Percentages are calculated from the number of patients who discontinued from screening.
[d] Percentages are calculated from the number of patients who were treated with study drug.
[e] Percentages are calculated from the number of patients who discontinued from treatment.
[f] Percentages are calculated from the number of patients who discontinued from study.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-1.1 - Patient Disposition
All Patients Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Screen Failures N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|---|
| Discontinued from study [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Primary reason for discontinuation [f] | | | | | | | | |
| Completed study | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Withdrawal by Patient | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Physician Decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lost to Follow-up | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Pregnancy | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Protocol Violation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Sponsor Request | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Protocol-Specified Withdrawal Criterion Met | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Patients who signed the informed consent.
[b] Percentages are calculated from the number of patients enrolled.
[c] Percentages are calculated from the number of patients who discontinued from screening.
[d] Percentages are calculated from the number of patients who were treated with study drug.
[e] Percentages are calculated from the number of patients who discontinued from treatment.
[f] Percentages are calculated from the number of patients who discontinued from study.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:
- Display all possible reasons, either reported for at least one subject or not.

Table 14.1-1.2 – Number of Patients in the Analysis Sets
All Patients Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Screen Failures N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|---|
| All Patients Set [a] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Full Analysis Set [b] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Safety Analysis Set [c] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Per Protocol Analysis Set [d] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Evaluable Analysis Set [e] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Patients who were enrolled regardless of whether they received the study drug or not.
[b] Patients who received at least 1 dose of the study drug.
[c] Patients who received at least 1 dose of the study drug.
[d] All patients from FAS who completed the study without any important protocol deviations.
[e] All patients from FAS who had the first efficacy evaluation on Study Day 29±3 and completed the study without any important protocol deviations.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.1-1.3 – Summary of Important Protocol Deviations
Full Analysis Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|
| Number of patients with at least one important protocol deviation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Deviation category 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Summary term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Summary term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Deviation category 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Summary term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Summary term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: A patient with multiple occurences of a protocol deviation is counted only once in this deviation category/summary term.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:
- Categories / Summary terms to match the PDCF.
- Present only important protocol deviations with at least one occurrence (where classification=Important).

Table 14.1-2.1 – Demographics and Baseline Characteristics
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Age (Years) | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XXX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |
| Age category (Years) n (%) | | | | | | | |
| 18 - 64 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 65 - 84 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| >=85 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Gender – n (%) | | | | | | | |
| Female | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Childbearing potential n (%) [a] | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Male | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Reproductive potential n (%) [a] | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Percentages are calculated from the number of patients within gender.
[b] Last non-missing value prior to first dose of study treatment.
[c] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.
[d] 0=Fully active, able to carry on all pre-disease performance without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2=Ambulatory and capable of all self-care but unable to carry out any work activities.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Table 14.1-2.1 - Demographics and Baseline Characteristics
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Race – n (%) | | | | | | | |
| American Indian or Alaska Native | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Asian | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Black or African American | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Native Hawaiian or Other Pacific Islander | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| White | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Ethnicity – n (%) | | | | | | | |
| Hispanic or Latino | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Hispanic or Latino | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Unknown | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Weight (kg) [b] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

[a] Percentages are calculated from the number of patients within gender.
[b] Last non-missing value prior to first dose of study treatment.
[c] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.
[d] 0=Fully active, able to carry on all pre-disease performance without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2=Ambulatory and capable of all self-care but unable to carry out any work activities.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Table 14.1-2.1 - Demographics and Baseline Characteristics
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Height (cm) [b] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| BMI at Baseline(kg/m^2) [c] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| ECOG performance at Baseline - n (%) [d] | | | | | | | |
| 0 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Smoking History - n (%) | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Current | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Former | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Percentages are calculated from the number of patients within gender.
[b] Last non-missing value prior to first dose of study treatment.
[c] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.
[d] 0=Fully active, able to carry on all pre-disease performance without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2=Ambulatory and capable of all self-care but unable to carry out any work activities.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Table 14.1-2.1 - Demographics and Baseline Characteristics
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Gene | | | | | | | |
| BRAF | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| MEK1/MAP2K1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| MEK2/MAP2K2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Codon | | | | | | | |
| G469 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Amino acid change | | | | | | | |
| Alanine A | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Arginine R | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other: xxxx | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Percentages are calculated from the number of patients within gender.
[b] Last non-missing value prior to first dose of study treatment.
[c] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.
[d] 0=Fully active, able to carry on all pre-disease performance without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2=Ambulatory and capable of all self-care but unable to carry out any work activities.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Table 14.1-2.1 - Demographics and Baseline Characteristics
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| NGS Vendor | | | | | | | |
| STRATA | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| FOUNDATION MEDICINE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| GUARDANT | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| CARIS | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| TEMPUS | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| OTHER | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Last non-missing value prior to first dose of study treatment.
[b] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.
[c] 0=Fully active, able to carry on all pre-disease performance without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2=Ambulatory and capable of all self-care but unable to carry out any work activities.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Table 14.1-2.2 – Disease History
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Cancer Diagnosis– n (%) | | | | | | | |
| Adenoid Cystic | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Anal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Appendiceal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Basal Cell Carcinoma of the Skin | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | | | | | | | |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Time since initial diagnosis (months) [a] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Disease stage at initial diagnosis – n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Calculated as (date of first dose of study treatment - date of diagnosis) / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-2.2 – Disease History
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Disease stage at enrollment – n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Method of diagnosis – n (%) | | | | | | | |
| Cytological | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Histological | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Prior Cancer Therapies/Regimens – n (%) | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Prior BRAF/MEK Inhibitor Therapies – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | | | | | | | |
| Prior Radiation Therapies – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | | | | | | | |

[a] Calculated as (date of first dose of study treatment - date of diagnosis) / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-2.3 – Summary of Medical History
Full Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any relevant medical history | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>.
If there is more than one medical history within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one medical history within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted by descending order of frequency for the overall group within primary SOC.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-2.4 – Summary of Concomitant Diseases
Full Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any relevant concomitant disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>.
If there is more than one concomitant disease within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one concomitant disease within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted by descending order of frequency for the overall group within primary SOC.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.1 – Prior Radiotherapies
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Received at least one prior radiotherapy - n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Total number of prior radiotherapies - n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Total number of prior radiotherapies by group | XX | XX | XX | XX | XX | XX | XX |
| Site of prior radiotherapy - n (%) [a] [b] | | | | | | | |
| Abdominal Cavity | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Adrenal Gland | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | | | | | | | |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Most recent prior radiotherapy before study treatment start | | | | | | | |
| Site of prior radiotherapy - n (%) | | | | | | | |
| Abdominal Cavity | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | | | | | | | |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Duration of therapy (months) [c] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

[a] Patients can have more than 1 site of prior radiotherapy if they had multiple prior radiotherapies.
[b] Percentages calculated from the total number of radiotherapies
[c] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)
BioMed Valley Discoveries Page 1 of Y
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Table 14.1-3.2 – Prior Anti-Cancer Therapies
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Received at least one prior anti-cancer Therapy - n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lines of prior anti-cancer therapies - n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Most recent therapy before study treatment start | | | | | | | |
| Regimen name - n (%) | | | | | | | |
| xxxxxxxx | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| xxxxxxxx | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| xxxxxxxx | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Regimen name sorted by decreasing frequency in the overall column.
[a] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.
[b] Calculated as [(date of first study treatment - date of BOR)+1] / 30.4375.
[c] Calculated as [(date of first study treatment - date of Relapse/Progression)+1] / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.2 – Prior Anti-Cancer Therapies
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Best Response - n (%) | | | | | | | |
| Complete Response | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Partial Response | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Stable Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Evaluable | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Done | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Duration of therapy (months) [a] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Time since Best Overall Response (months) [b] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

[a] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.
[b] Calculated as [(date of first study treatment - date of BOR)+1] / 30.4375.
[c] Calculated as [(date of first study treatment - date of Relapse/Progression)+1] / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.2 – Prior Anti-Cancer Therapies
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Time since Relapse/Progression (months) [c] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Reason for discontinuation – n (%) | | | | | | | |
| Intolerance | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lack of Efficacy (incl. PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Completed Therapy | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.
[b] Calculated as [(date of first study treatment - date of BOR)+1] / 30.4375.
[c] Calculated as [(date of first study treatment - date of Relapse/Progression)+1] / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.3 – Prior BRAF/MEK inhibitor therapies
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Received at least one prior BRAF/MEK inhibitor therapy - n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Prior BRAF/MEK inhibitor therapies - n (%) | | | | | | | |
| Vemurafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Dabrafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Encorafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Trametinib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Most recent therapy before study treatment start | | | | | | | |
| BRAF/MEK inhibitor therapies - n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Vemurafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Dabrafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Encorafenib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Based on tumor alteration groups, only patients from Groups 5 and 6 are expected to have prior BRAF/MEK inhibitor therapies.
[a] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.
[b] As collected from the CRF page: Prior BRAF/MEK inhibitor therapies.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.3 – Prior BRAF/MEK inhibitor therapies
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Best Response – n (%) | | | | | | | |
| Complete Response | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Partial Response | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Stable Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Evaluable | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Done | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Duration of therapy (months) [a] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Duration of Response (months) [b] | XX | XX | XX | XX | XX | XX | XX |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Reason for discontinuation – n (%) | | | | | | | |
| Intolerance | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Lack of Efficacy (incl. PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Completed Therapy | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Based on tumor alteration groups, only patients from Groups 5 and 6 are expected to have prior BRAF/MEK inhibitor therapies.
[a] Calculated as [(end date of therapy - start date of therapy)+1] / 30.4375.
[b] As collected from the CRF page: Prior BRAF/MEK inhibitor therapies.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)
Filename: (Specify file name.rtf)

Table 14.1-3.4 – Prior Medications
Full Analysis Set

| ATC Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any Prior Medications | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| ATC class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| ATC class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: WHOHD-B3 <vx.x>. ATC=Anatomical Therapeutic Chemical.
If there is more than one medication within an ATC class, the patient is counted only once under that ATC class. If there is more than one medication within an ATC class and preferred term (PT), the patient is counted only once in that ATC class and PT.
ATC classes are presented by descending order of frequency for the overall group, PTs are sorted by descending order of frequency for the overall group within ATC class.
Prior medication is defined as any medications whose end date is before the first study treatment date.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-3.5 – Concomitant Medications
Full Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.1-3.4
- Present concomitant medications.
- Replace footnote 'Prior medication is defined as…' with the following footnote:
  'Concomitant medication is defined as any medication ongoing at first day of study drug or started after first day of study drug up to the end of the on-treatment period.'

Table 14.1-4.1 – Treatment exposure
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Number of cycles received [a] – n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |
| Duration of exposure to ulixertinib (months) [b] – n (%) | | | | | | | |
| < 1 month | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1-2 months | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2-3 months | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |

[a] Number of cycles received = Number of cycles where the patient received at least one dose.
[b] Duration of exposure (months) = [(Date of last known treatment dosing with ulixertinib – date of initial dosing with ulixertinib) + 1] / 30.4375.
[c] Actual cumulative dose received (mg) = Sum of [(number of capsules dispensed – number of capsules returned) x 150.
[d] Relative dose intensity = 100 x Actual dose intensity / Planned dose intensity. Actual dose intensity (mg/day) is defined as Actual cumulative dose received (mg) / Duration of exposure (days). Planned dose intensity (mg/day) is defined as Planned cumulative dose (mg) / Duration of exposure (days).
Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-4.1 – Treatment exposure
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Actual cumulative dose on ulixertinib (mg) [c] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |
| Relative dose intensity [d] | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |

[a] Number of cycles received = Number of cycles where the patient received at least one dose.
[b] Duration of exposure (days) = (Date of last known treatment dosing with ulixertinib – date of initial dosing with ULIXERTINIB) + 1.
[c] Actual cumulative dose received (mg) = Sum of [(number of capsules dispensed – number of capsules returned) x 150.
[d] Relative dose intensity = 100 x Actual dose intensity / Planned dose intensity. Actual dose intensity (mg/day) is defined as Actual cumulative dose received (mg) / Duration of exposure (days). Planned dose intensity (mg/day) is defined as Planned cumulative dose (mg) / Duration of exposure (days).

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.1-4.2 – Dosing Interruptions and Adjustments
Full Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| At least one dose change – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Reason dose changed – n (%) [a] | | | | | | | |
| Adverse event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Parental/Guardian decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Consent withdrawal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | | | | | | | |
| Dose changed to – n (%) [b] | | | | | | | |
| 150mg BID | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 300mg BID | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 450mg BID | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 600mg BID | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| At least one dose interruption – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Reason dose interrupted [a] | | | | | | | |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Dispensing Error | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Investigator Decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Consent Withdrawal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patient Decision | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Other | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

[a] A patient can be counted under several reasons if they had multiple different dose changes/interruptions.
[b] A patient can be counted under more than one dose level if they had multiple different dose changes.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.2-1.1.1 – Best Overall Response and Overall Response Rate
Full Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Best overall response – n (%) [a] | | | | | | | |
| Complete response (CR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Partial response (PR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Stable disease (SD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive disease (PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not evaluable (NE) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Overall response rate (CR+PR) – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 95 % CI for Overall response rate | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) |
| Disease Control Rate (CR+PR+SD) – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 95 % CI for Overall response rate | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) | (XX.X, XX.X) |
| Non responders (SD+PD+NE) – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: CI=Confidence Interval.
95% CI is estimated using the Clopper-Pearson method.
[a] Confirmed Best overall response as per RECIST 1.1

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.2-1.1.2 – Best Overall Response and Overall Response Rate
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.1.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.1.3 – Best Overall Response and Overall Response Rate
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.1.1
- Present data on Evaluable Analysis Set.

Table 14.2-1.2.1 – Overall, Target and Non-Target Lesion Response
Full Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| C1D28 | | | | | | | |
| Target Lesion Response – n (%) | | | | | | | |
| Complete response (CR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Partial response (PR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Stable disease (SD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive disease (PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not evaluable (NE) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Non-Target Lesion Response – n (%) | | | | | | | |
| Complete response (CR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Non-Complete Response/Non Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive disease (PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Applicable | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Overall Response – n (%) | | | | | | | |
| Complete response (CR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Partial Response (PR) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Stable Disease (SD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Progressive disease (PD) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Evaluable (NE) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| *Programming Note: Repeat for all available assessments* | | | | | | | |

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)
Filename: (Specify file name.rtf)

Table 14.2-1.2.2 – Overall, Target and Non-Target Lesion Response
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.2.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.2.3 – Overall, Target and Non-Target Lesion Response
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.2.1
- Present data on Evaluable Analysis Set.

Table 14.2-1.3.1 – Incidence of New Lesions
Full Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| C1D28 | | | | | | | |
| New Lesions – n (%) | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Number of New Lesions – n (%) | | | | | | | |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| … | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |

*Programming Note: Repeat for all available assessments*

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)
Filename: (Specify file name.rtf)

Table 14.2-1.3.2 – Incidence of New Lesions
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.3.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.3.3 – Incidence of New Lesions
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.3.1
- Present data on Evaluable Analysis Set.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY



Table 14.2-1.4.1 - Duration of Response
Full Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Patients with response (CR+PR) - n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients with events - n (%) [a] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients censored - n (%) [a] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Duration of response (months) [b] | | | | | | | |
| Median (95% CI) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |
| Min, Max | XX, XX* | XX, XX | XX, XX | XX, XX* | XX, XX | XX, XX* | XX, XX |
| KM probability estimates for duration of response (95% CI) [c] | | | | | | | |
| 3 Months | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |
| 6 Months | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |
| 9 Months | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |
| 12 Months | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |
| 18 Months | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) | XX<br>(X.X, X.X) |

Note: CI=Confidence Interval, CR=Complete Response, PR=Partial Response.
Duration of response is the period from the date of initial PR or CR until the date of first radiographically documented progressive disease or death from any cause.
[a] Percentage calculated on patients with response. Events are death or disease progression.
[b] Product-limit (Kaplan-Meier) estimates. 95% CI for median calculated using the Brookmeyer and Crowley method.
[c] Based upon Kaplan-Meier (KM) estimates and 95% CI use the log-log transformation.
* Censored observation at maximum value.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Table 14.2-1.4.2 – Duration of Response
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.4.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.4.3 – Duration of Response
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.4.1
- Present data on Evaluable Analysis Set.

Table 14.2-1.5.1 – Progression-Free Survival (PFS)
Full Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Patients with events – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients censored – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| PFS (months) [a] | | | | | | | |
| Median (95% CI) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| Min, Max | XX, XX* | XX, XX | XX, XX | XX, XX* | XX, XX | XX, XX* | XX, XX |
| KM probability estimates for PFS (95% CI) [b] | | | | | | | |
| 3 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 6 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 9 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 12 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 18 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |

Note: CI=Confidence Interval.
Progression-Free Survival (PFS) is the time from the first ulixertinibdose until the first radiographically documented progression of disease or death from any cause, whichever occurs first.
[a] Product-limit (Kaplan-Meier) estimates. 95% CI for median calculated using the Brookmeyer and Crowley method.
[b] Based upon Kaplan-Meier (KM) estimates and 95% CI use the log-log transformation.
* Censored observation at maximum value.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.2-1.5.2 – Progression-Free Survival (PFS)
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.5.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.5.3 – Progression-Free Survival (PFS)
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.5.1
- Present data on Evaluable Analysis Set.

Table 14.2-1.6.1 – Overall Survival (OS)
Full Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Patients with events – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients censored – n (%) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| OS (months) [a] | | | | | | | |
| Median (95% CI) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| Min, Max | XX, XX* | XX, XX | XX, XX | XX, XX* | XX, XX | XX, XX* | XX, XX |
| KM probability estimates for PFS (95% CI) [b] | | | | | | | |
| 3 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 6 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 9 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 12 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |
| 18 Months | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) | XX (X.X, X.X) |

Note: CI=Confidence Interval.
Overall Survival (OS) is the time from the first ulixertinib dose until death from any cause.
[a] Product-limit (Kaplan-Meier) estimates. 95% CI for median calculated using the Brookmeyer and Crowley method.
[b] Based upon Kaplan-Meier (KM) estimates and 95% CI use the log-log transformation.
* Censored observation at maximum value.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)
Filename: (Specify file name.rtf)

Table 14.2-1.6.2 – Overall Survival (OS)
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.6.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.2-1.6.3 – Overall Survival (OS)
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.2-1.6.1
- Present data on Evaluable Analysis Set.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.3-1.1 – Overview Summary of Treatment-Emergent Adverse Events
Safety Analysis Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|
| Number of patients with: | | | | | | | |
| Any TEAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any SAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related SAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment discontinuation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment discontinuation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment discontinuation within 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment discontinuation within 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment discontinuation following 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment discontinuation following 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment interruption | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment interruption | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment interruption within 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment interruption within 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to treatment interruption following 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to treatment interruption following 1 cycle | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: SAE=Serious Adverse Events, TEAE=Treatment-Emergent Adverse Events

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Table 14.3-1.1 – Overview Summary of Treatment-Emergent Adverse Events
Safety Analysis Set

| | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Number of patients with: | | | | | | | |
| Any TEAE leading to dose reduction | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any related TEAE leading to dose reduction | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to dose reduction within Cycle 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to dose reduction within Cycle 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to dose reduction following Cycle 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to dose reduction following Cycle 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE leading to death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE leading to death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any TEAE with Grade >= 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Any Related TEAE with Grade >= 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: SAE=Serious Adverse Events, TEAE=Treatment-Emergent Adverse Events

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Table 14.3-1.2 – Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any TEAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>. TEAE=Treatment-Emergent Adverse Events.
If there is more than one TEAE within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one TEAE within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted by descending order of frequency for the overall group within each SOC.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.3-1.3 – Summary of Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.2
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.4 – Summary of Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.2
- Present Serious TEAE: TEAEs with SAE =" Yes".
- Add footnote:
  "Serious TEAE: TEAEs with SAE =" Yes"."

Table 14.3-1.5 – Summary of Related Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.2
- Present Related Serious TEAE: SAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "SAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.6 – Summary of Treatment-Emergent Adverse Events by Preferred Term
Safety Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any TEAE | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | | | | | | | |

Note: MedDRA <vx.x>. TEAE=Treatment-Emergent Adverse Events.
If there is more than one TEAE within a preferred term (PT), the patient is counted only once in that PT.
PTs are sorted in descending order of frequency for the overall group.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.3-1.7 – Summary of Related Treatment-emergent Adverse Events by Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.6
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.8 – Summary of Serious Treatment-emergent Adverse Events by Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.6
- Present Serious TEAE: TEAEs with SAE =" Yes".
- Add footnote:
  "Serious TEAE: TEAEs with SAE =" Yes"."

Table 14.3-1.9 – Summary of Related Serious Treatment-emergent Adverse Events by Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.6
- Present Related Serious TEAE: SAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "SAEs with causality=Related, Possibly Related or missing."

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.3-1.10 – Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term for Maximum CTCAE Grade
Safety Analysis Set

Group: Group X

| System Organ Class<br>Preferred Term | Any CTC Grade<br>n (%) [Events] | CTC Grade 1<br>n (%) | CTC Grade 2<br>n (%) | CTC Grade 3<br>n (%) | CTC Grade 4<br>n (%) | CTC Grade 5<br>n (%) |
|---|---|---|---|---|---|---|
| Any TEAE | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) [XX] | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>; CTCAE v5.0. TEAE=Treatment-Emergent Adverse Events.
If there is more than one TEAE within a system organ class (SOC), the patient is counted only once under that SOC and maximum severity.
If there is more than one TEAE within a SOC and preferred term (PT), the patient is counted only once in that SOC, PT and maximum severity.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted within primary SOC descending order of frequency for the overall group within each SOC.
[Events] presents the number of TEAEs reported overall, by primary SOC and PT regardless of severity.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Present for each group and overall.

Table 14.3-1.11 – Summary of Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term for Maximum CTCAE Grade
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.10
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.12 – Summary of Treatment-Emergent Adverse Events Leading to Treatment Discontinuation
by System Organ Class and Preferred Term
Safety Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any TEAE leading to treatment discontinuation | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>. TEAE=Treatment-Emergent Adverse Events.
If there is more than one TEAE leading to treatment discontinuation within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one TEAE leading to treatment discontinuation within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted within primary SOC descending order of frequency for the overall group within each SOC.
TEAEs leading to treatment discontinuation: any TEAEs with Action taken with study treatment=Drug withdrawn.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.3-1.13 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Discontinuation
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.12
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.14 – Summary of Treatment-Emergent Adverse Events Leading to Treatment Discontinuation Within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.12
- Add footnote:
  "TEAEs leading to treatment discontinuation: any TEAEs with Action taken with study treatment=Drug withdrawn within the first 28 days of study."

Table 14.3-1.15 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Discontinuation Within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.12
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "TEAEs leading to treatment discontinuation: any TEAEs with Action taken with study treatment=Drug withdrawn within the first 28 days of study."

Table 14.3-1.16 – Summary of Treatment-Emergent Adverse Events Leading to Treatment Discontinuation Following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Add footnote:
  "TEAEs leading to treatment discontinuation: any TEAEs with Action taken with study treatment=Drug withdrawn after the first 28 days of study."
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.17 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Discontinuation Following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.'
- Add footnote:
  "TEAEs leading to treatment discontinuation: any TEAEs with Action taken with study treatment=Drug withdrawn after the first 28 days of study."
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.18 – Summary of Treatment-Emergent Adverse Events Leading to Treatment Interruption
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to treatment interruption.'
- Add footnote:
- "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted'.

Table 14.3-1.19 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Interruption
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to treatment interruption.'
- Add footnotes:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted'.
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.20 – Summary of Treatment-Emergent Adverse Events Leading to Treatment Interruption Within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to treatment interruption within Cycle 1.'
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted' within the first 28 days of study.

Table 14.3-1.21 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Interruption Within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to treatment interruption within Cycle 1.'
- Add footnotes:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted' after the first 28 days of study.

Table 14.3-1.22 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Interruption Following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to treatment interruption following Cycle 1.'
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted' after the first 28 days of study.
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.23 – Summary of Related Treatment-Emergent Adverse Events Leading to Treatment Interruption Following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to treatment interruption following Cycle 1'.
- Add footnotes:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Interrupted' after the first 28 days of study.
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.24 – Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to dose reduction.'
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced'".

Table 14.3-1.25 – Summary of Related Treatment-Emergent Adverse Events Leading to Dose Reduction
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to dose reduction.'
- Add footnotes:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced'".
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.26 – Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to dose reduction within Cycle 1.'
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced' within the first 28 days of study".

Table 14.3-1.27 – Summary of Related Treatment-Emergent Adverse Events Leading to Dose Reduction within Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to dose reduction within Cycle 1.'
- Add footnotes:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced' within the first 28 days of study".
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.28 – Summary of all Treatment-Emergent Adverse Events Leading to Dose Reduction following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any TEAE leading to dose reduction following Cycle 1.
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced' after the first 28 days of study".

Table 14.3-1.29 – Summary of Related Treatment-Emergent Adverse Events Leading to Dose Reduction following Cycle 1
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.12
- Replace 'Any TEAE' by 'Any related TEAE leading to dose reduction following Cycle 1.
- Add footnote:
  "Includes TEAE with 'Action Taken with treatment' = 'Dose Reduced' after the first 28 days of study".
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.30 – Summary of Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term
Safety Analysis Set

| System Organ Class<br>Preferred Term | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Any TEAE leading to death | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| System organ class 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Preferred term 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: MedDRA <vx.x>. TEAE=Treatment-Emergent Adverse Events.
If there is more than one TEAE leading to death within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one TEAE leading to death within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT.
Primary SOCs are presented by descending order of frequency for the overall group, PTs are sorted within primary SOC descending order of frequency for the overall group within each SOC.
TEAEs leading to Death: any TEAE resulting in death, Outcome=Fatal, CTC Grade=5.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.3-1.31 – Summary of Related Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat Table 14.3-1.20
- Present Related TEAE: TEAEs with causality=Related, Possibly Related or missing.
- Add footnote:
  "Related TEAE: TEAEs with causality=Related, Possibly Related or missing."

Table 14.3-1.32 – Summary of Deaths
All Patients Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Screen Failures N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|---|
| Patients who died during the study | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Primary cause of death | | | | | | | | |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Unknown | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Patients who died after taking the first dose of ulixertinib | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Primary cause of death | | | | | | | | |
| Progressive Disease | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Adverse Event | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Unknown | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Table 14.3-2.1 – Summary and Change from Baseline in Hematology Laboratory Results by Visit
Safety Analysis Set

Parameter: XXXXX (XX)

| Visit<br>Statistics | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Baseline | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Change from Baseline to C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all hematology parameters: hematocrit, hemoglobin, platelets, red blood cells (RBC), white blood cells (WBC), neutrophil absolute, basophil absolute, monocyte absolute, lymphocyte absolute and eosinophil absolute with respective unit measure.
- Present for all available visits.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.3-2.2.1 – Gradable Hematology Laboratory Results – Worst On-treatment Value by Cycle
Safety Analysis Set

| Parameter (unit)<br>Cycle<br>CTCAE Grade | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| XXXXX (XXX) | | | | | | | |
| Cycle 1 | | | | | | | |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Missing | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Cycle 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Missing | | | | | | | |
| … | | | | | | | |

Note: CTCAE v5.0.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all hematology parameters where CTCAE grades are defined as per the SAP appendix 14.2.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.3-2.2.2 – Non-gradable Hematology Laboratory Results – Worst On-treatment Value by Cycle
Safety Analysis Set

| Parameter (unit)<br>Cycle<br>CTCAE Grade | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| XXXXX (XXX) | | | | | | | |
| Cycle 1 | | | | | | | |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Low | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| High | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Missing | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Cycle 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Low | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| High | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Missing | | | | | | | |
| … | | | | | | | |

Note: CTCAE v5.0.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all hematology parameters where CTCAE grades are **not** defined as per the SAP appendix 14.2.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Table 14.3-2.3.1 – Shift Table of Gradable Hematology Laboratory Results – Baseline vs Worst On-treatment Value
Safety Analysis Set

Part A
Group: Group 1

| Parameter (unit) | Baseline Grade | Worst CTCAE grade during treatment period | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Normal n (%) | 1 n (%) | 2 n (%) | 3 n (%) | 4 n (%) | Missing n (%) | Total n (%) |
| XXXXX (XXX) | Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Missing | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Total | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: CTCAE v5.0.
Baseline is the last available assessment prior to first dose of study treatment.
Percentages are based on the number of patients in the group.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Present for each group and overall, and for all hematology parameters where CTCAE grades are defined as per the SAP appendix 14.2.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Table 14.3-2.3.2 – Shift Table of Non-gradable Hematology Laboratory Results – Baseline vs Worst On-treatment Value
Safety Analysis Set

Part A
Group: Group 1

| Parameter (unit) | Baseline Grade | Worst grade during treatment period: Low n (%) | Normal n (%) | High n (%) | Missing n (%) | Total n (%) |
|---|---|---|---|---|---|---|
| XXXXX (XXX) | Low | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | High | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Missing | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Total | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Baseline is the last available assessment prior to first dose of study treatment.
Percentages are based on the number of patients in the group.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Present for all groups and overall, and for all hematology parameters where CTCAE grades are not defined as per the SAP appendix 14.2.

Table 14.3-2.4 – Summary and Change from Baseline in Biochemistry Laboratory Results by Visit
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.3-2.1
- Present for all biochemistry parameters: alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, blood urea nitrogen, calcium, chloride, cholesterol, creatinine, direct bilirubin, glucose, indirect bilirubin, inorganic phosphorus, lactate dehydrogenase, potassium, total protein, sodium, total bilirubin, triglycerides, uric acid.
- Present for all available visits.

Table 14.3-2.5.1 – Gradable Biochemistry Laboratory Results – Worst On-treatment Value by Cycle
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat of Table 14.3-2.2.1
- Present for all biochemistry parameters where CTCAE grades are defined as per the SAP appendix 14.2.

Table 14.3-2.5.2 – Non-gradable Biochemistry Laboratory Results – Worst On-treatment Value by Cycle
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat of Table 14.3-2.2.2
- Present for all biochemistry parameters where CTCAE grades are defined as per the SAP appendix 14.2.

Table 14.3-2.6.1 – Shift Table of Gradable Biochemistry Laboratory Results – Baseline vs Worst On-treatment Value
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat of Table 14.3-2.3.1
- Present for all groups and overall, and for all biochemistry parameters where CTCAE grades are defined as per the SAP appendix 14.2.

Table 14.3-2.6.2 – Shift Table of Non-gradable Biochemistry Laboratory Results – Baseline vs Worst On-treatment Value
Safety Analysis Set

**PROGRAMMING NOTES:**

- Repeat of Table 14.3-2.3.2
- Present for all groups and overall, and for all biochemistry parameters where CTCAE grades are not defined as per the SAP appendix 14.2.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Table 14.3-2.7 – Summary and Change from Baseline in Urinalysis Laboratory Results by Visit
Safety Analysis Set

Parameter: Specific gravity (XX)

| Visit<br>Statistics | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Baseline | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Change from Baseline to C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Table 14.3-2.7 – Summary and Change from Baseline in Urinalysis Laboratory Results by Visit
Safety Analysis Set

Parameter: Blood (XX)

| Visit<br>Statistics | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Baseline | | | | | | | |
| Negative | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| C1D1 | | | | | | | |
| Negative | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4+ | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

<cont.>

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- present for all urinalysis parameters: specific gravity, pH, dipstick evaluation of glucose, dipstick evaluation of protein, dipstick evaluation of bilirubin, dipstick evaluation of ketones, dipstick evaluation of leukocytes, dipstick evaluation of blood, microscopic examination of RBC, microscopic examination of WBC, microscopic examination of casts.
- Present for all available visits.

Table 14.3-3.1 – Summary and Change from Baseline in Vital Signs by Visit
Safety Analysis Set

Parameter: XXXXX (XX)

| Visit<br>Statistics | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Baseline | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| Change from Baseline to C1D8 | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all vital signs: systolic blood pressure, diastolic blood pressure, pulse and temperature with respective unit measure.
- Present for all available visits.

Table 14.3-3.2 – Shift Table of Vital Signs Results – Baseline vs Worst On-treatment Value
Safety Analysis Set

Group: Group 1

| Parameter (unit) | Baseline Value | Worst value during on-treatment period: Low n (%) | Normal n (%) | High n (%) | Very High n (%) | Missing n (%) | Total n (%) |
|---|---|---|---|---|---|---|---|
| XXXXX (XXX) | Low | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | High | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Very High | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Missing | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| | Total | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Baseline is the last available assessment prior to first dose of study treatment.
Percentages are based on the number of patients in the group.
For Temperature, Low: < 36.4°C, Normal: 36.4°C - 37.7°C, High: > 37.7°C.
For Pulse, Low: < 55 bpm, Normal: 55-100 bpm, High: 101-150 bpm, Very high: > 150 bpm.
For Systolic blood pressure, Low: < 90 mmHg, Normal: 90-130 mmHg, High: 131-160 mmHg, Very high: ≥ 161 mmHg.
For Diastolic blood pressure, Low: < 60 mmHg, Normal: 60-85 mmHg, High: 86-100 mmHg, Very high: ≥ 101 mmHg.
Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Present for each group and overall, and for all vital signs parameters.

Data extraction date: DDMMMYYYY

Table 14.3-3.3 – Summary of ECG at Baseline
Safety Analysis Set

| | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Heart Rate | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| PR Interval | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |
| QRS Duration | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all ECG parameters: heart rate, PR interval, QRS duration, RR interval, QT interval, QTcF with respective unit measure.

Table 14.3-3.4 – Summary of ECHO/MUGA at Baseline
Safety Analysis Set

| | Group 1 N=XX | Group 2 N=XX | Group 3 N=XX | Group 4 N=XX | Group 5 N=XX | Group 6 N=XX | Overall N=XX |
|---|---|---|---|---|---|---|---|
| Method – n (%) | | | | | | | |
| Echocardiography | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| MUGA | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Significant findings – n (%) | | | | | | | |
| Yes | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| No | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| LVEF | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) | XX.X (XX.XX) |
| Median | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X | XX.X |
| Min; Max | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX | XX; XX |

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Table 14.3-3.5 – Summary of Physical Examination at Baseline
Safety Analysis Set

| | Group 1 N=XX n (%) | Group 2 N=XX n (%) | Group 3 N=XX n (%) | Group 4 N=XX n (%) | Group 5 N=XX n (%) | Group 6 N=XX n (%) | Overall N=XX n (%) |
|---|---|---|---|---|---|---|---|
| HEENT | | | | | | | |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Abnormal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Done | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Thorax | | | | | | | |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Abnormal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Done | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Abdomen | | | | | | | |
| Normal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Abnormal | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| Not Done | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

<cont.>

Note: Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present for all Region/Body System parameters: HEENT, thorax, abdomen, skin and mucosae, neurological, extremities, urogenital, general appearance, heart, back, lymph nodes.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY
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BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Table 14.3-3.6 – Summary of ECOG Performance Status by Visit
Safety Analysis Set

| Visit<br>Grade | Group 1<br>N=XX<br>n (%) | Group 2<br>N=XX<br>n (%) | Group 3<br>N=XX<br>n (%) | Group 4<br>N=XX<br>n (%) | Group 5<br>N=XX<br>n (%) | Group 6<br>N=XX<br>n (%) | Overall<br>N=XX<br>n (%) |
|---|---|---|---|---|---|---|---|
| Baseline [a] | | | | | | | |
| 0 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| C1D8 [a] | | | | | | | |
| 0 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 1 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 2 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 3 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 4 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| 5 | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| C1D15 [a] | | | | | | | |
| …… | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |
| <cont.> | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) | XX (XX.X) |

Note: Baseline is the last available assessment prior to first dose of study treatment.
[a] (0) Fully active, able to carry on all pre-disease performance without restriction
(1) Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
(2) Ambulatory and capable of all self-care but unable to carry out any work activities
(3) Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
(4) Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
(5) Death

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Present for all available visits.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

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Table 14.5-1.1 – Pharmacokinetic Data
Full Analysis Set

| Visit<br>Analyte | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Cycle X Day Y | | | | | | | |
| BVD-523 (ng/mL) | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XXX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Geometric Mean (CV) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XXX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |

CV=Coefficient of Variation, SD=Standard Deviation

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.doc)

**PROGRAMMING NOTES:**

- Present for all available analytes (BVD-523, BVD-502/503,BVD-506, BVD-513) and visits

Table 14.5-1.2 – Pharmacokinetic Data
Per Protocol Set

**PROGRAMMING NOTES:**
- Repeat Table 14.5-1.1
- Present data on Per Protocol Set.
- For Part B only

Table 14.5-1.3 – Pharmacokinetic Data
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Repeat Table 14.5-1.1
- Present data on Evaluable Analysis Set.

Table 14.6-1.1 – Blood Pharmacodynamic Data
Full Analysis Set

| Visit<br>Analyte | Group 1<br>N=XX | Group 2<br>N=XX | Group 3<br>N=XX | Group 4<br>N=XX | Group 5<br>N=XX | Group 6<br>N=XX | Overall<br>N=XX |
|---|---|---|---|---|---|---|---|
| Cycle X Day Y<br>% inhibition (simplified to 0-100%) | | | | | | | |
| n | XX | XX | XX | XX | XX | XX | XX |
| Mean (SD) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XXX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) | XX.XX (XX.XX) |
| Median | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX | XX.XX |
| Min; Max | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X | XX.X; XX.X |

GSD=Geometric Standard Deviation, SD=Standard Deviation

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.doc)

Figure 14.2-1.1 – Consort Diagram
Full Analysis Set

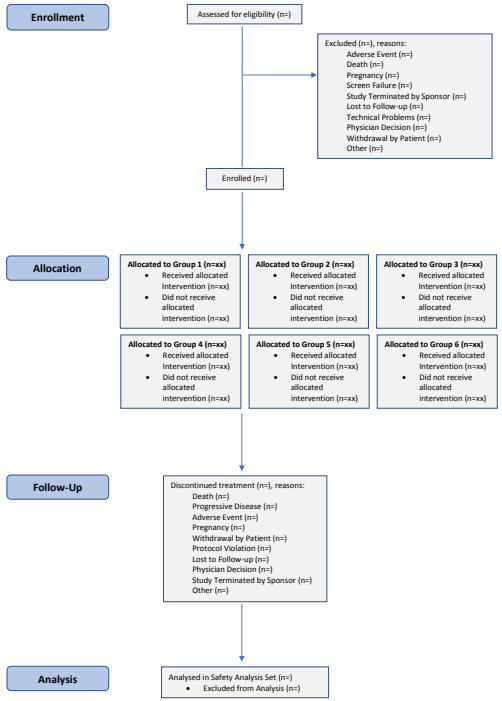
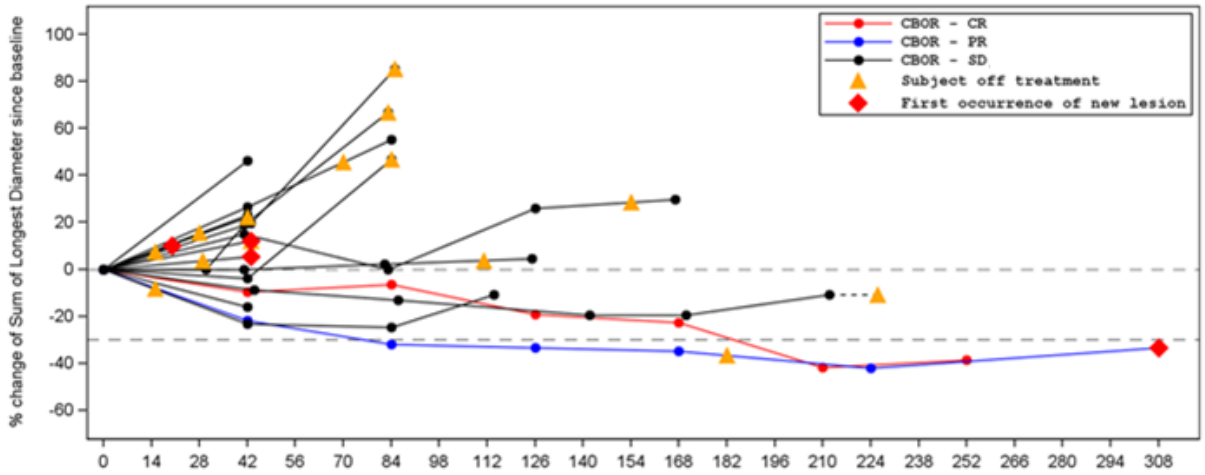


Figure 14.2-1.2.1 – Spider plot of Percentage Change from Baseline in Sum of Longest Diameter
Full Analysis Set

Group = Group X




Weeks since Treatment Initiation

Best overall response: CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progression Disease, NE=Not Evaluable.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present all groups from Part A in separate figures and one figure with all patients.
- Use a different color style for each BOR separately (CR/PR/SD/PD/NE).
- Add reference lines for +20% and -30%.

Figure 14.2-1.2.2 – Spider plot of Percentage Change from Baseline in Sum of Longest Diameter Per Protocol Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.2.1
- Present data on Per Protocol Set.

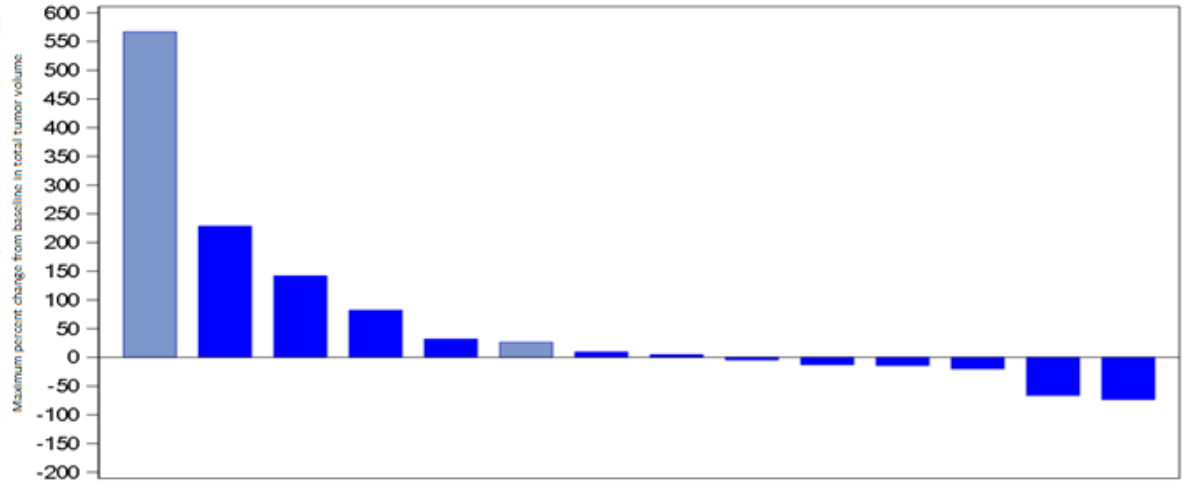
Figure 14.2-1.2.3 – Spider plot of Percentage Change from Baseline in Sum of Longest Diameter Evaluable Analysis Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.2.1
- Present data on Evaluable Analysis Set.

Figure 14.2-1.3.1 – Waterfall plot of Maximum Percentage Change from Baseline in Sum of Longest Diameter
Full Analysis Set

Group = Group X




Maximum percentage change from baseline in total tumor size is the maximum percent change in the sum of longest diameters/short axis for all target lesions observed from baseline for each patient.

Best overall response: CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progression Disease, NE=Not Evaluable.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present each group from Part A on one figure and one figure with all patients.
- Each bar is an individual patient.
- Add reference lines for +20% and -30%.
- Add the best overall response (CR, PR, SD, PD, NE) of each patient on the top of each bar.

Figure 14.2-1.3.2 – Waterfall plot of Maximum Percentage Decrease from Baseline in Sum of Longest Diameter Per Protocol Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.3.1
- Present data on Per Protocol Set.

Figure 14.2-1.3.3 – Waterfall plot of Maximum Percentage Decrease from Baseline in Sum of Longest Diameter Evaluable Analysis Set

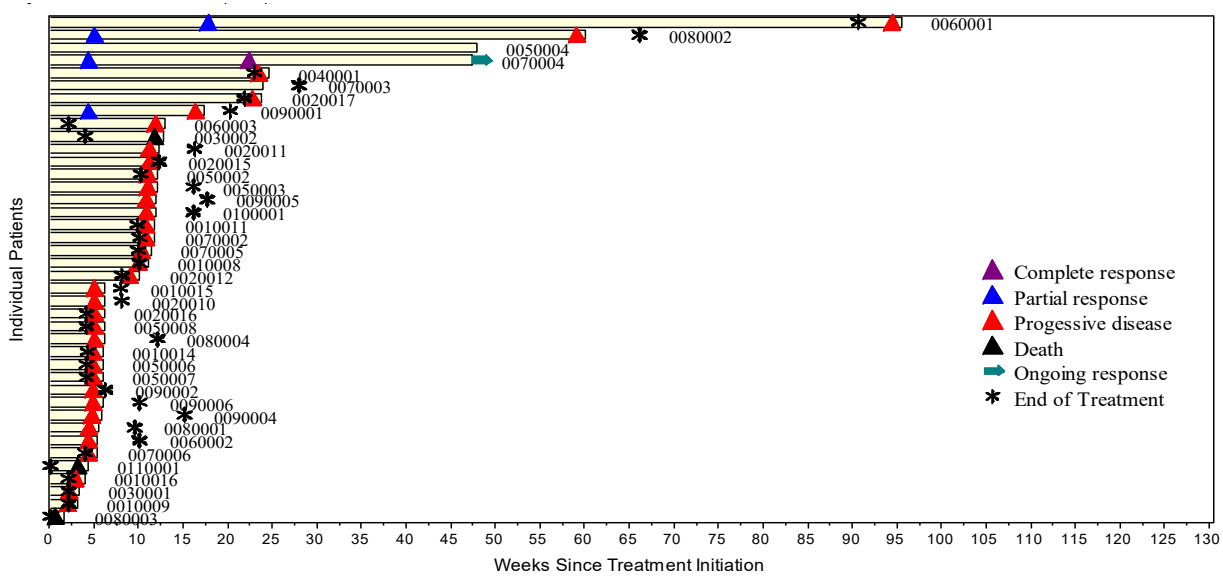
**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.3.1
- Present data on Evaluable Analysis Set.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Figure 14.2-1.4.1 – Swimmer Plot of Response Assessments
Full Analysis Set




Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Present each group from Part A on one figure and a figure including all patients.
- Display patient ID on the left outside the figure.
- The bar displays time to PD/Death (PFS), with "PD" or "death" displayed at the end of the bar; if no PD/death occurred before cutoff date, the bar stops at cutoff date.
- For responders, display the date of first CR or PR, and display "Ongoing response" arrow if no PD or death occurred before cutoff date.
- "End of Treatment" is the date of treatment discontinuation, this must be displayed only for patients who discontinued the treatment before the cut-off date.

Figure 14.2-1.4.2 – Swimmer Plot of Response Assessments
Per Protocol Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.4.1
- Present data on Per Protocol Set.

Figure 14.2-1.4.3 – Swimmer Plot of Response Assessments
Evaluable Analysis Set

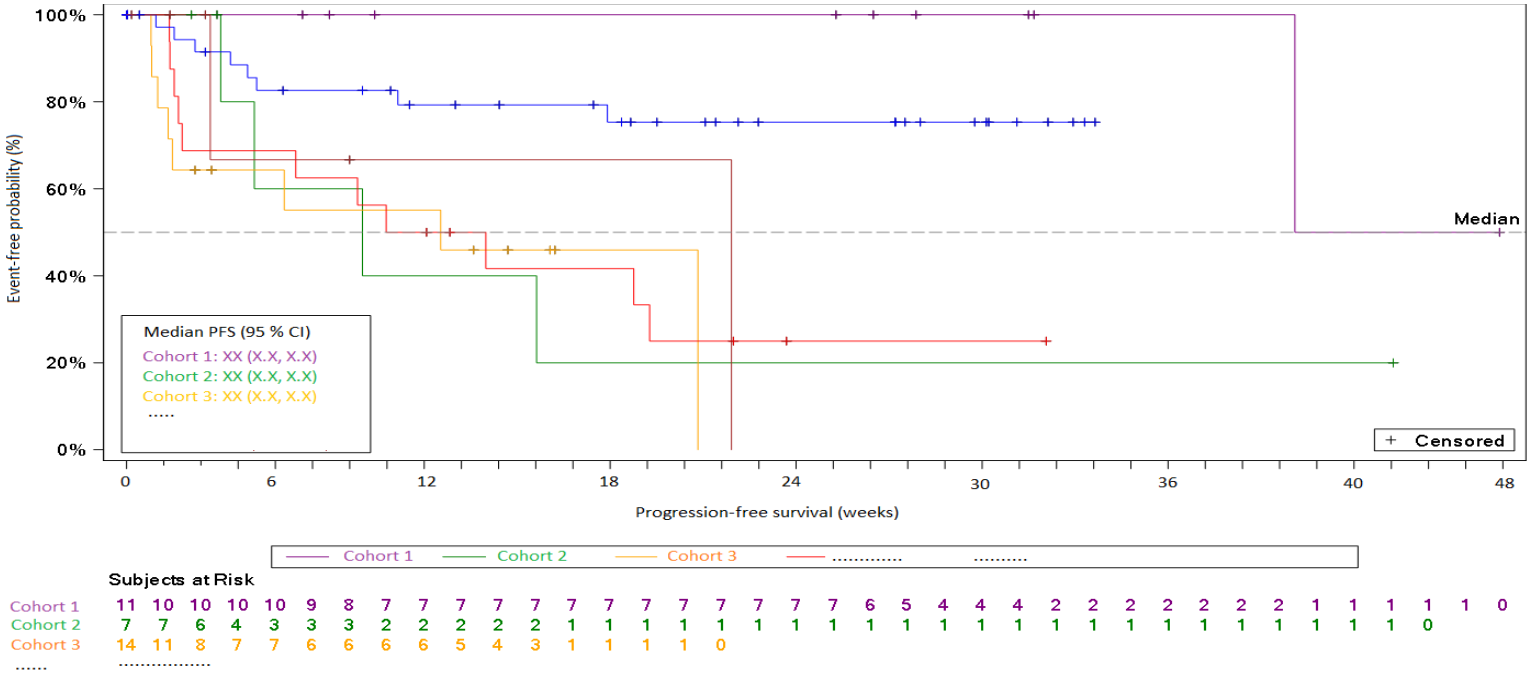
**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.4.1
- Present data on Evaluable Analysis Set.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Figure 14.2-1.5.1 – Kaplan-Meier Estimate for Duration of Response
Full Analysis Set




Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- X-axis – Label "Duration of Response (months)"
- Y-axis – Label "Event-free probability (%)."
- Legend: overall number of events, "Median Duration of Response" and 95% CI.
- Flag censored observations with '+' and add legend.
- If the median time to event has not been reached, present as "Median (95% CI) NR (xx.x, xx.x)" [replacing xx.x with '-' if there is no upper or lower confidence limit] and add footnote:
  NR=Median time not reached.
- For Part A, present all groups on the same figure but with different colors and separate figures for each group.

Figure 14.2-1.5.2 – Kaplan-Meier Estimate for Duration of Response
Per Protocol Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.5.1
- Present data on Per Protocol Set.

Figure 14.2-1.5.3 – Kaplan-Meier Estimate for Duration of Response
Evaluable Analysis Set

**PROGRAMMING NOTES:**

- Repeat Figure 14.2-1.5.1
- Present data on Evaluable Analysis Set.

Figure 14.2-1.6.1 – Kaplan-Meier Estimate for Progression-Free survival (PFS)
Full Analysis Set

**PROGRAMMING NOTES:**

- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Progression Free Survival" in X-axis label and legend.

Figure 14.2-1.6.2 – Kaplan-Meier Estimate for Progression-Free survival (PFS)
Per Protocol Set

**PROGRAMMING NOTES:**
- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Progression Free Survival" in X-axis label and legend.
- Present data on Per Protocol Set.

Figure 14.2-1.6.3 – Kaplan-Meier Estimate for Progression-Free survival (PFS)
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Progression Free Survival" in X-axis label and legend.
- Present data on Evaluable Analysis Set.

Figure 14.2-1.7.1 – Kaplan-Meier Estimate for Overall Survival
Full Analysis Set

**PROGRAMMING NOTES:**
- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Overall Survival" in X-axis label and legend.

Figure 14.2-1.7.2 – Kaplan-Meier Estimate for Overall Survival
Per Protocol Set

**PROGRAMMING NOTES:**
- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Overall Survival" in X-axis label and legend.
- Present data on Per Protocol Set.

Figure 14.2-1.7.3 – Kaplan-Meier Estimate for Overall Survival
Evaluable Analysis Set

**PROGRAMMING NOTES:**
- Replicate figure 14.2-1.5.1, replacing "Duration of Response" by "Overall Survival" in X-axis label and legend.
- Present data on Evaluable Analysis Set.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY

Listing 16.2.1-1 - Patients informed consent
All Patients Set

Group: Group 1

| | | | Main Informed Consent | | Sample banking for future Biospecimen research consent | | Optional End of Treatment Biopsy | | Pregnancy and Pregnant Partner | |
|---|---|---|---|---|---|---|---|---|---|---|
| Subject ID | Age / Gender | Protocol Version | Consent Obtained / Withdrawn? | Date Consent Obtained / Withdrawn | Consent Obtained / Withdrawn? | Date Consent Obtained / Withdrawn | Consent Obtained / Withdrawn? | Date Consent Obtained / Withdrawn | Consent Obtained? | Date Consent Obtained / Withdrawn |
| XXXXXX | XX/M | 1.0 | Yes / Yes | DDMMMYYYY / DDMMMYYYY | Yes | DDMMMYYYY / DDMMMYYYY | Yes | DDMMMYYYY / DDMMMYYYY | Yes | DDMMMYYYY / DDMMMYYYY |
| XXXXXX | XX/F | 1.0 | Yes / No | DDMMMYYYY | Yes | DDMMMYYYY | Yes | DDMMMYYYY | Yes | DDMMMYYYY |
| XXXXXX | XX/F | 1.0 | Yes / No | DDMMMYYYY | Yes | DDMMMYYYY | Yes | DDMMMYYYY | Yes | DDMMMYYYY |
| XXXXXX | XX/F | 1.0 | No / Yes | DDMMMYYYY DDMMMYYYY | No | DDMMMYYYY | No | DDMMMYYYY | No | DDMMMYYYY |

<cont.>

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.doc)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY

Listing 16.2.1-2 - Failed Inclusion and Exclusion Criteria
All Patients Set

Group: Group 1

| Subject ID | Age / Gender | Protocol Version | Failed Inclusion / Exclusion No. | Description |
|---|---|---|---|---|
| xxx-xx | xx/M | 1.0 | INCL01 | xxxxxxxxxxxx |
| xxx-xx | xx/M | 1.0 | EXCL01 | xxxxxxxxxxxx |
| xxx-xx | xx/M | 1.0 | EXCL02 | xxxxxxxxxxxx |
| xxx-xx | xx/F | 1.0 | INCL02 | xxxxxxxxxxxx |

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- List all failed Inclusion / Exclusion criteria as per eCRF.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.1-3 – Patient Disposition
All Patients Set

Group: Group 1

| Subject ID | Age / Gender | Enrolled | Date of Assignment | Gene/ Codon/ Amino acid change | Completed Screening / Reason | Date of Screening Completion / Discontinuation | Eligible for inclusion? | Rescreened? / Previous patient number |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | DDMMMYYYY | BRAF /D594 / Alanine A | Yes | DDMMMYYYY | Yes | No |
| xxx-xx | xx/F | Yes | DDMMMYYYY | MEK1/MAP2K1 / K601 /Arginine R | No / Physician Decision | DDMMMYYYY | Yes | Yes /xxxxxxx |

Enrolled patients are patients that fullfill all selection criterion and included in the study to be dosed.
Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.1-3 - Patient Disposition
All Patients Set

Group: Group 1

| Subject ID | Age / Gender | Completed Treatment / Reason | Date of Treatment Discontinuation | Date of Last Study Dose | Completed Study / If no, reason | Date of Completion (Follow-up) / Discontinuation from Study |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | DDMMMYYYY | DDMMMYYYY | Yes | Yes |
| xxx-xx | xx/F | No/ Progressive Disease | DDMMMYYYY | DDMMMYYYY | No/ xxxxxx | Yes |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.1-4 – Randomization
Full Analysis Set

| Subject ID | Randomization Number | Allocated treatment |
|---|---|---|
| xxx-xx | xxxxx | Ulixertinib - Group X |
| xxx-xx | xxxxx | Physician's Choice |
| xxx-xx | xxxxx | |
| xxx-xx | xxxxx | |

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.2-1 – Analysis Sets
All Patients Set

Part A
Group: Group 1

| Subject ID | Age / Gender | All Patients Set [a] | Full Analysis Set [b] | Safety Analysis Set [c] | Per Protocol Analysis Set [d] | Evaluable Analysis Set [e] |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Yes | Yes | Yes | Yes |
| xxx-xx | xx/F | Yes | Yes | Yes | Yes | Yes |

Note: M=Male, F=Female.
[a] Patients who were enrolled regardless of whether they received the study drug or not.
[b] Patients who received at least 1 dose of the study drug.
[c] Patients who received at least 1 dose of the study drug.
[d] All patients from FAS who completed the study without any important protocol deviations.
[e] All patients from FAS who had the first efficacy evaluation on Study Day 29+3 and completed the study without any important protocol deviations.
Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries Page 1 of Y
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.3-1 – Protocol Deviations
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Deviation Category | Summary Term | Deviation Description | Important? | Exclusion from Analysis Sets |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Inclusion Criteria … | xxxxxxxxxxxx | xxxxxxxxxxxx | Non-Important | Safety Analysis Set |
| xxx-xx | xx/F | Study Assessments … | xxxxxxxxxxxx | xxxxxxxxxxxx | Important | Full Analysis Set |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:
- Categories / Summary Term / Description to match the PDCF.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY



Listing 16.2.4-1 - Demographics and Baseline Characteristics
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Childbearing/ Reproductive Potential | Surgery Name | Date of Surgery/Post-Menopausal | Date of Last Menstrual Period | Race | Ethnicity | Height at Screening (cm) | Weight at Screening (kg) | BMI at Screening (kg/m^2) [a] |
|---|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Surgically Sterile | Vasectomy | DDMMMYYY | | White | Hispanic or Latino | xx | xx | xx |
| xxx-xx | xx/F | Able to Bear Children | | | DDMMMYYY | Other, xxxx | Not Hispanic or Latino | xx | xx | xx |
| xxx-xx | xx/F | Sterile - Other Reason, xxxxxx | | | DDMMMYYY | | | | | |

Note: M=Male, F=Female.
[a] Body Mass Index (BMI)=Weight (kg)/ Height(m)^2.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Listing 16.2.4-2 - Smoking History
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Smoking History? | Substance | Usage |
|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Cigarettes | Former |
| xxx-xx | xx/F | No | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY



Listing 16.2.4-3 - Disease History
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Cancer Diagnosis | Date of Initial Diagnosis | Time since Initial Diagnosis [a] | Stage at Diagnosis | Method of Diagnosis | Current Stage at Enrollment | Prior Cancer Therapies/ Regimens? | Prior BRAF/MEK Inhibitor Therapies? | Prior Radiation Therapies? |
|---|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Stomach | DDMMMYYYY | xx | 1 | Cytological | 1 | Yes | No | Yes |
| xxx-xx | xx/F | Other, xxxxx | DDMMMYYYY | xx | 2 | Histological | 4 | No | No | No |

Note: M=Male, F=Female.
[a] Presented in months and calculated as (date of first study treatment - date of diagnosis) / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:

- For all cases where 'Other' is present, please present the respective 'Other' specification.

Listing 16.2.4-4 – Medical History and Concomitant Diseases
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Reported Term | System Organ Class | Preferred Term | Start Date (Day) /End Date (Day) | Ongoing | MH or Conc. |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | xxxxxxxx | xxxxxxxxx | xxxxxxxx | DDMMMYYYY (xx) / DDMMMYYYY (xx) | No | MH |
| xxx-xx | xx/F | xxxxxxxx | xxxxxxxxx | xxxxxxxx | DDMMMYYYY (xx) | Yes | Conc. |

Note: M=Male, F=Female.
MedDRA <vx.x>.
Medical history (MH): any conditions that started before the first study treatment date and were not ongoing at the first study treatment date.
Concomitant disease (Conc.): any conditions that started before first study treatment administration and were ongoing at first study treatment administration.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries Page 1 of Y
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.4-5 – Prior Anti-Cancer Therapies
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Line of Therapy | Name of Therapy | Start Date (Day) | End Date (Day) | Best Overall Response | Date of Best Overall Response | Date of Relapse/ Progression | Reason for Discontinuation |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | 1 | xxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Stable Disease | DDMMMYYYY | DDMMMYYYY | Intolerance |
| xxx-xx | xx/M | 1 | xxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Stable Disease | DDMMMYYYY | DDMMMYYYY | Lack of Efficacy |
| xxx-xx | xx/F | 4 | xxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Partial Response | DDMMMYYYY | DDMMMYYYY | Other, xxxxx |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:
- Data taken from 'Prior Cancer Medications' page.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.4-6 – Prior BRAF/MEK Inhibitor Therapies
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Prior BRAF/MEK inhibitor therapies | Start Date (Day) | End Date (Day) | Best Response | Duration of Response (unit) | Reason for Discontinuation |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Vemurafenib | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Stable Disease | xx (xxx) | Intolerance |
| xxx-xx | xx/M | Dabrafenib | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Stable Disease | xx (xxx) | Completed Therapy |
| xxx-xx | xx/F | Other, xxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Partial Response | xx (xxx) | Other, xxxxx |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:

- Data taken from 'Prior BRAF/MEK inhibitor therapies' page.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.4-7 – Prior Radiation Therapies
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Site of Radiotherapy | Dose (Unit) | Start Date (Day) | End Date (Day) | Duration (months) [a] |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Abdominal Cavity | xxx (xxx) | DDMMMYYYY (xx) | DDMMMYYYY (xx) | xx |
| xxx-xx | xx/M | Adrenal Gland | xxx (xxx) | DDMMMYYYY (xx) | DDMMMYYYY (xx) | xx |
| xxx-xx | xx/F | Bile Duct | xxx (xxx) | DDMMMYYYY (xx) | DDMMMYYYY (xx) | xx |

Note: M=Male, F=Female.
[a] Duration of radiotherapy calculated as [(end date – start date) + 1] / 30.4375.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Data taken from 'Prior Radiotherapy' page.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.4-8 – Prior and Concomitant Medications
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Reported Term / Preferred Term / ATC Class | Indication | Start Date (Day) | End Date (Day) | Dose (Units) / Frequency | Route | Medication to treat adverse event? / Adverse Event (ID) | Ongoing | Prior / Conc. |
|---|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Xxxxxxxxxx / xxxxxxxxxxx / xxxxxx | xxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | xxx (xx) / Daily | Oral | Yes / xxxx (x) | Yes | Conc. |
| xxx-xx | xx/F | xxxxxxxxxx/ xxxxxxxxxxx / xxxxxx | xxxxxx | DDMMMYYYY (xx) | Ongoing | xxx (xx) / Twice per day | Oral, xxxx | No | No | Prior |

Note: M=Male, F=Female, ATC=Anatomical Therapeutic Chemical.
WHOHD-B3 <vx.x>.
Prior medication (Prior): any medications whose end date is before the first study treatment date.
Concomitant medication (Conc.): any medication whose start or end date is either the same or after the first dose of study treatment and up to the end of the on-treatment period.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES**:
- Data taken from 'Prior and Concomitant Medications' page.
- Adverse Event ID taken from collected ID.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.4-9 – On Treatment Radiation
Full Analysis Set

Cohort: Group 1

| Subject ID | Age / Gender | Received Radiation? | Site of Radiotherapy | Dose (Unit) | Start Date (Day) | End Date (Day) |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Abdominal Cavity | xxx (xxx) | DDMMMYYYY (xx) | DDMMMYYYY (xx) |
| xxx-xx | xx/M | Yes | Adrenal Gland | xxx (xxx) | DDMMMYYYY (xx) | DDMMMYYYY (xx) |
| xxx-xx | xx/F | No | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Data taken from 'On Treatment Radiation' page.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.4-10 – On Treatment Surgery and Medical Procedures
Full Analysis Set

Cohort: Group 1

| Subject ID | Age / Gender | Any Surgeries/ Procedures | Name of Surgery/ Procedure | Indication? | Start Date (Day) | End Date (Day) | Ongoing? |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | xxxxxxxxxx | xxxxxxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | No |
| xxx-xx | xx/M | Yes | xxxxxxxxxx | xxxxxxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Yes |
| xxx-xx | xx/F | No | | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Data taken from 'On Treatment Surgery and Medical Procedures' page.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.4-11 – On Treatment Blood Transfusions
Full Analysis Set

Cohort: Group 1

| Subject ID | Age/ Gender | Any blood transfusions | Transfusion ID | Date of Transfusion | Category of Transfusion | Units |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | xxxxxxxxxx | DDMMMYYYY (xx) | Platelet transfusion | xx |
| | xx/M | Yes | xxxxxxxxxx | DDMMMYYYY (xx) | Plasma | xx |
| xxx-xx | xx/F | No | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Data taken from 'On Treatment Blood Transfusions' page.

Listing 16.2.4-12 – NGS Data
Full Analysis Set

Cohort: Group 1

| Subject ID | Age/ Gender | Gene / Codon / Amino acid change | Vendor | Date of Report | Report Redacted | Report Uploaded |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | BRAF /D594 / Alanine A | STRATA | DDMMMYYYY (xx) | Yes | Yes |
| xxx-xx | xx/F | MEK1/MAP2K1 / K601 /Arginine R | GUARDANT | | No | No |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.5-1 – Drug Administration
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Treatment Administered? | Dose (mg) | Dose Date and Time (day) | Dose Adjusted? / Reason |
|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | xxx | DDMMMYYYY hh:mm (xx) | Yes / Adverse event |
| xxx-xx | xx/F | Yes | xxx | DDMMMYYYY hh:mm (xx) | No |
| xxx-xx | xx/F | Yes | Xxx | DDMMMYYYY hh:mm (xx) | Yes / Other, xxxx |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.5-2 – Dosing Interruptions and Changes
Full Analysis Set

Part A
Group: Group 1

| Subject ID | Age / Gender | Type of Change | Start Date / End Date / Duration (days) | If Adjustment, new dose amount (mg) | Reason for Interruption/Adjustment |
|---|---|---|---|---|---|
| xxx-xx | xx/M | Interruption | DDMMMYYYY / DDMMMYYYY / (xx) | xxx | Adverse Event |
| xxx-xx | xx/F | Adjustment | DDMMMYYYY / DDMMMYYYY / (xx) | xxx | Other, xxxxx |
| xxx-xx | xx/F | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.5-3 – Drug Exposure
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Number of cycles received [a] | Duration of exposure (months) [b] | Planned cumulative dose (mg) | Actual cumulative dose received (mg) [c] | Relative dose intensity [d] |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | xx | xxx | xxx (mg) | xxx (mg) | xxx |
| xxx-xx | xx/F | xx | xxx | xxx (mg) | xxx (mg) | xxx |

Note: M=Male, F=Female.
[a] Number of cycles received = Number of cycles where the patient received at least one dose.
[b] Duration of exposure (months) = (Date of last known treatment dosing with ulixertinib– date of initial dosing with ulixertinib) + 1 / 30.4375.
[c] Actual cumulative dose received (mg) = Sum of [(number of capsules dispensed – number of capsules returned) x 150].
[d] Relative dose intensity = 100 x Actual dose intensity / Planned dose intensity. Actual dose intensity (mg/day) is defined as Actual cumulative dose received (mg) / Duration of exposure (days). Planned dose intensity (mg/day) is defined as Planned cumulative dose (mg) / Duration of exposure (days).

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

Listing 16.2.5-3 – Study Drug Dispensed
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Mg prescribed per dose | Date Bottles Dispensed (day) | Number of Bottles Dispensed | Lot Number of the bottles dispensed | Different Lot number dispensed to the patient? | Lot number dispensed to patient /No of bottles | Total Number of Capsules Dispensed |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | xxx | DDMMMYYYY (xx) | xx | xxxx | Yes | xxxx | xx |
| xxx-xx | xx/F | xxx | DDMMMYYYY (xx) | xx | xxxx | No | xxxx | xx |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') - Part X
Data extraction date: DDMMMYYYY



Listing 16.2.5-4 - Study Drug Returned
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Cycle | Reason capsules not returned | Date Returned (day) | Patient compliant since last visit? If no, reason | Missed dose related to an adverse event? | Number of Bottles Returned | Lot Number of the bottles returned | Total Number of Capsules Returned |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | 2 | Lost | DDMMMYYYY (xx) | Yes | Yes | xx | xxxx | xxx |
| xxx-xx | xx/F | 3 | Other, xxxxx | DDMMMYYYY (xx) | No, xxxxx | Yes | xx | xxxx | xxx |

Note: M=Male, F=Female.
Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X >)
Data extraction date: DDMMMYYYY



Listing 16.2.6-1 – Target Lesions
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Visit | Assessment Performed / Reason | Target Lesions at Screening? | Lesion Number | Tumor Type | Organ Site | Method | Date of Scan (Day) | Longest Diameter/ Short-axis(mm) | Sum of Longest Diameter (mm) / Change from baseline / % Change from baseline |
|---|---|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | Yes | T01 | Primary | Bladder | CT Scan | DDMMMYYYY (xx) | xxx | xxx |
| | | C2D1 | No, xxxx | | | | | | | | |
| | | … | | | | | | | | | |
| xxx-xx | xx/F | Screening | Yes | Yes | T02 | Metastasis | Other, xxxxx | MRI | DDMMMYYYY (xx) | xxx | xxx / xxx / xxx |
| | | … | | | | | | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.6-2 – Non-Target Lesions
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Visit | Assessment Performed / Reason | Non-Target Lesions at screening | Lesion Number | Organ Site | Method | Date of Scan (Day) | Result |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | Yes | NT01 | Bladder | CT Scan | DDMMMYYYY (xx) | Present |
| | | C2D1 | No, xxx | | | | | | |
| | | … | | | | | | | |
| xxx-xx | xx/F | Screening | Yes | Yes | NT02 | Other, xxxx | MRI | DDMMMYYYY (xx) | Absent (Disappeared) |
| | | … | | | | | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, visit.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.6-3 – New Lesions
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Visit | Any New Lesions | Lesion Number | Method | Date of Scan (Day) | Organ Site |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | C2D29 | Yes | NL01 | CT Scan | DDMMMYYYY (xx) | Abdomen |
| xxx-xx | xx/F | C2D29 | Yes | NL02 | Other, xxxx | DDMMMYYYY (xx) | Bone |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.6-4 – Overall Response
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Best Overall Response [a] | Assessment Performed/ Reason | Date of Assessment (Day) | Target Lesion Response | Non-Target Lesion Response | New Lesions | Overall Response |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | CR | Yes | DDMMMYYYY (xx) | CR | CR | Yes | CR |
| xxx-xx | xx/F | PD | Yes | DDMMMYYYY (xx) | NE | PD | No | NE, xxxx |

Note: M=Male, F=Female, CR=Complete Response, Non CR/Non PD=Non Complete Response/Non Progressive Disease, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, NE=Not Evaluable.
[a] Confirmed best overall response.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.6-5 – Duration of Response (DOR)
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Best Overall Response [a] | Treatment Start Date | Date of First Response | Date of Last Tumor Assessment | Date of Event / Censoring | Event / Censoring Reason | Duration of Response (months) |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | CR | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | Death | xx.x |
| xxx-xx | xx/F | PR | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | Censored: xxxxx | xx.x |

Note: M=Male, F=Female, CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, NE=Not Evaluable.
Event: progressive disease (PD) or death from any cause.
This listing includes only patients with response (CR or PR).
[a] Confirmed best overall response.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.6-6 – Progression-Free Survival (PFS)
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Treatment Start Date | Date of Last Tumor Assessment | Date of Event/ Censoring | Event / Censoring Reason | PFS (months) |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | Death | xx.x |
| xxx-xx | xx/F | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY | Censored: xxxxx | xx.x |

Note: M=Male, F=Female, PFS=Progression-Free Survival.
Event: progressive disease (PD) or death from any cause.
The PFS (in months) is defined as the time from the first ulixertinib dose until the first radiographically documented progression of disease or death from any cause, whichever occurs first.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.6-7 – Survival Status
Full Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Completed End of Study? | Any Anti-Cancer Treatment Since End of Study or Last FUP/ Start Date | Any Tumor Assessment Since End of Study or Last FUP/ Assessment Date/ Overall Response | Survival Status at Follow-Up | Date of Death | Last Known Date Patient Alive [a] |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Yes/ DDMMMYYYY | Yes/ DDMMMYYYY/ Complete Response | Alive | | |
| xxx-xx | xx/F | Yes | No | No | Dead | DDMMMYYYY | |

Note: M=Male, F=Female, FUP=Follow-up, CR=Complete Response, Non CR/Non PD=Non Complete Response/Non Progressive Disease, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, NE=Not Evaluable.
[a] If Survival status at the time of follow-up is unknown.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

Listing 16.2.7-1 – Adverse Events
All Patients Set

Group: Group 1

| Subject ID | Age / Gender | ID | Reported Term | System Organ Class | Preferred Term | Start Date (day) | End Date (day) | TEAE? | SAE? |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | xx | xxxxxxxxx | xxxxxxxxx | xxxxxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | Yes | Yes |
| xxx-xx | xx/F | xx | xxxxxxxxx | xxxxxxxxx | xxxxxxxxx | DDMMMYYYY (xx) | DDMMMYYYY (xx) | No | No |

Note: M=Male, F=Female, TEAE=Treatment Emergent Adverse Event, SAE=Serious Adverse Event.
ID as collected in the databased.
MedDRA <vx.x>. NCI CTCAE v5.0.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.7-2 – Treatment-Emergent Adverse Events
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | ID | Reported Term / System Organ Class /Preferred Term | Start Date (Day) / End Date (Day) / Duration (days) | SAE / Seriousness | NCI-CTCAE Grade | Relation Ship to Disease / Ulixertinib | Action Taken with Ulixertinib | Medication or Therapies? / Medication Name | Outcome [a] |
|---|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | xx | xxxxxxxx/ xxxxxxxxx/ xxxxxxxxx … | DDMMMYYYY (xx) / DDMMMYYYY (xx) / xx | Yes / Hospitalization | 1 | Related /Related | Drug Interrupted | Yes /xxxxxxxx, xxxxxxx | Res'd |
| xxx-xx | xx/F | xx | xxxxxxxx/ xxxxxxxxx/ xxxxxxxxx … | DDMMMYYYY (xx) / DDMMMYYYY (xx) / xx | No | 3 | Possibly Related /Related | Drug Interrupted | Yes /xxxxxxxx | Res'd seq, xxxxxx |

Note: M=Male, F=Female, TEAE=Treatment Emergent Adverse Event, SAE=Serious Adverse Event.
MedDRA <vx.x>. NCI CTCAE v5.0.
ID as collected in the databased.
[a] Res'd=Resolved, Res'd seq=Recovered/Resolved with sequelae, Ong=Ongoing, Unk=Unknown, Fatal=Fatal.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, ascending Adverse Event Start Date and Reported Term.
- Outcome = "Res'd seq" please specify sequelae.

Listing 16.2.7-3 – Serious Adverse Events
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Listing 16.2.7-2 and include only AEs classified as Serious.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.7-4 – Deaths
All Patients Set

Group: Group 1

| Subject ID | Age / Gender | Date of Death (Day) | Autopsy Performed? / Date of Autopsy | Primary Cause of Death | Treatment-Emergent Death [a] |
|---|---|---|---|---|---|
| xxx-xx | xx/M | DDMMMYYYY (xx) | No | Progressive Disease | Yes |
| xxx-xx | xx/F | DDMMMYYYY (xx) | Yes /DDMMMYYYY | Adverse Event, xxxxxxx | No |

Note: M=Male, F=Female.
[a] A death is considered Treatment-Emergent if occurred after Ulixertinib administration.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Specify primary cause of death if not PD.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.8-1 – Hematology
Safety Analysis Set

Group: Group 1

| Subject ID | Age/ Gender | Study Visit | Sample Date and Time (Day) | Laboratory Name | Parameter (Unit) | Result / Reference Range Indicator / CS? | LLN – ULN | CTC Grade | Change from Baseline |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | DDMMMYYYY / hh:mm (xx) | xxxxxxxx | RBC (xxx) | xx / L / CS | xx – xx | xx | |
| | | | | | … | | | | |
| | | C1D1 | DDMMMYYYY / hh:mm (xx) | xxxxxxxx | RBC (xxx) | xx / L / CS | xx – xx | xx | xx |
| | | … | | | … | | | | |
| xxx-xx | xx/F | Screening | DDMMMYYYY / hh:mm (xx) | xxxxxxxx | RBC (xxx) | Not Done | | | |
| | | | | | … | | | | |
| | | C1D1 | | | | | | | |
| | | … | | | | | | | |

Note: M=Male, F=Female, L=Low, H=High, ULN=Upper Limit of Normal, LLN=Lower Limit of Normal, CS=Clinically Significant, NCS=Non Clinically Significant.
CTCAE v5.0.
Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Sort by group, subject ID, ascending Sample Date and Time and Parameter.
- Include all hematology parameters.

Listing 16.2.8-2 – Biochemistry
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Listing 16.2-8.1 for all biochemistry parameters.

Listing 16.2.8-3 – Urinalysis
Safety Analysis Set

**PROGRAMMING NOTES:**
- Repeat Listing 16.2-8.1 for all urinalysis parameters.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.8-4 – Pregnancy
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Sample Type | Assessment Performed? /Reason | Sample Date (Day) | Result |
|---|---|---|---|---|---|---|
| xxx-xx | xx/F | Screening<br>Baseline | Serum | Yes | DDMMMYYYY (xx) | Positive |
| xxx-xx | xx/F | Screening | Serum | No /xxxxx | | |

Note: M=Male, F=Female.
Baseline is the last available assessment prior to first dose of study treatment.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, visit.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.9-1 – Vital Signs
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Assessment Performed? / Reason | Assessment Date and Time (Day) | Parameter (Unit) | Result/ Reference Range Indicator / CS? [a] | Position | Change from baseline |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | DDMMMYYYY hh:mm (xx) | Systolic Blood Pressure (xxx) | xx / H / CS | Sitting | |
| | | | | | … | | | |
| | | Baseline | Yes | DDMMMYYYY hh:mm (xx) | Systolic Blood Pressure (xxx) | xx / H / CS | Supine | |
| | | … | | | … | | | |
| xxx-xx | xx/F | Screening | No / xxxxxx | | | Not Done | | |
| | | … | | | | | | |

Note: M=Male, F=Female, L=Low, H=High, VH=Very High, ND=Not Done, CS=Clinically Significant, NCS=Non Clinically Significant.
[a] If status = "Not Done" populate with "Not Done".
* Baseline is the last available assessment prior to first dose of study treatment.
For temperature, Low if < 36.4°C; high if > 37.7°C.
For pulse, Low if < 55bpm; high if 101-150bpm; very high if > 150bpm.
For systolic blood pressure, Low if < 90mmHg; high if 131-160mmHg; very high if >= 161mmHg.
For diastolic blood pressure, Low if < 60mmHg; high if 86-100mmHg; very high if >= 101mmHg.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Sort by group, subject ID, ascending Assessment Date and Time and Parameter.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.9-2 – Electrocardiogram
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Assessment Performed? / Reason | Assessment Date and Time | Method/ Position | Parameter (Unit) | Result /CS? | Change from baseline |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | DDMMMYYYY hh:mm | 12 Lead Standard/ Supine | Heart Rate (xxx) | xx /No | |
| xxx-xx | xx/F | Screening | Yes | DDMMMYYYY hh:mm | 12 Lead Standard/ Supine | Heart Rate (xxx) | xx /Yes | |

Note: M=Male, F=Female, L=Low, H=High.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, ascending Assessment Date and Time and Parameter.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.9-3 – ECHO/MUGA
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Assessment Performed? / Reason | Method | Assessment Date (Day) | Parameter (Unit) | Result /CS? |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Echocardiography | DDMMMYYYY (xx) | LVEF (xx) | xx /No |
| xxx-xx | xx/F | No /xxxx | MUGA | DDMMMYYYY (xx) | LVEF (xx) | xx |

Note: M=Male, F=Female, LVEF=Left Ventricular Ejection Fraction.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, ascending Assessment Date and Time.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.9-4 – Physical Examination
Safety Analysis Set

Part A
Group: Group 1

| Subject ID | Age / Gender | Study Visit | Assessment Performed? / Reason | Assessment Date | Region /Body System | Result /CS? [a] | Abnormal Findings |
|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | DDMMMYYYY | HEENT | Abnormal/ CS | xxxxxxx |
| xxx-xx | xx/F | Screening | Yes | DDMMMYYYY | Thorax | Not Done | |

Note: M=Male, F=Female, CS=Clinically Significant, NCS=Non Clinically Significant.
[a] If status = "Not Done" populate with "Not Done".

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, visit.

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.9-5 – Ophthalmology Exam
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Assessment Performed? / Reason | Assessment Date | Any Abnormal Clinically Significant Result? | Examination Test Name | Side | Abnormal Finding |
|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | DDMMMYYYY | Yes | Best-corrected visual acuity … | Left | xxxxxxxxxxx |
| xxx-xx | xx/F | Screening | Yes | DDMMMYYYY | No | | | |

Note: M=Male, F=Female, CS=Clinically Significant, NCS=Non Clinically Significant.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, visit.

Listing 16.2.9-6 – Meals
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Meal Consumed with Dose Administration? | Meal Consumed | Meal Date | Meal Start Time | Meal End Time |
|---|---|---|---|---|---|---|
| xxx-xx | xx/M | Yes | Breakfast | DDMMMYYYY | xx.xx | xx.xx |
| xxx-xx | xx/F | Yes | Lunch | DDMMMYYYY | xx.xx | xx.xx |

Note: M=Male, F=Female

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

BioMed Valley Discoveries 
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY

Listing 16.2.9-7 – ECOG Performance Status
Safety Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Assessment Performed? / Reason | Date of Assessment (Day) | ECOG Performance Status [a] |
|---|---|---|---|---|---|
| xxx-xx | xx/M | Screening | Yes | DDMMMYYYY (xx) | (0) Fully Active |
| | | Baseline | Yes | DDMMMYYYY (xx) | (0) Fully Active |
| | | … | | | |
| xxx-xx | xx/F | Screening | Yes | DDMMMYYYY (xx) | (1) Restricted |
| | | Baseline | No, xxxx | | |
| | | … | | | |

Note: M=Male, F=Female.
Baseline is the last available assessment prior to first dose of study treatment.
[a] (0) Fully active, able to carry on all pre-disease performance without restriction
(1) Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
(2) Ambulatory and capable of all self-care but unable to carry out any work activities
(3) Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
(4) Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
(5) Death

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM) Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**
- Sort by group, subject ID, visit, assessment date.

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.10-1 – Blood Pharmacodynamic Data
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Collection Date/Time (Day) / Timepoint | Ulixertinib dose at the time of sample collection | Patient at Steady state? | Condition Specifics | Parameter | Result | Comments |
|---|---|---|---|---|---|---|---|---|---|
| xxx-xx | xx/M | C1D1 | ddmmmyyyy hh:mm (xx) / Pre-dose | 600mg BID | Yes | PMA (day 1, predose) | % Inhibition simplified (0-100%) | xxxx | xxxxxxxx |
| | | | ddmmmyyyy hh:mm (xx) / 4-hours post dose | 450mg BID | Yes | PMA (day1, Cmax) | % Inhibition simplified (0-100%) | xxxxx | xxxxxxxx |
| | | … | | | | | | | |

**PROGRAMMING NOTES:**

- Sort by group, subject ID, visit, assessment date and time

BioMed Valley Discoveries
Protocol: BVD-523-ABC ('Delivery' / 'Type') – Part X
Data extraction date: DDMMMYYYY



Listing 16.2.11-1 – Pharmacokinetic Data
Full Analysis Set

Group: Group 1

| Subject ID | Age / Gender | Study Visit | Ulixertinib dose at the time of sample collection | Patient at Steady state? | Collection Date/Time (Day) / Timepoint | Analyte | Concentration (Unit) |
|---|---|---|---|---|---|---|---|
| | | | | | | | xxxx (ng/mL) |
| xxx-xx | xx/M | C1D15 | 600mg BID | Yes | ddmmmyyyy hh:mm (xx) / Pre-dose | BVD-523 | |
| | | | 450mg BID | Yes | | | |

Note: M=Male, F=Female.

Program: (Program name.sas) (run on: DDMMMYYYY HH:MM)

Filename: (Specify file name.rtf)

**PROGRAMMING NOTES:**

- Sort by group, subject ID, visit, assessment date and time.

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Document Pages: 188
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dsousamanteigas@cmedresearch.com
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| Signer Events | Signature | Timestamp |
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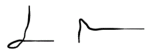
| David Sousa Manteigas<br>dsousamanteigas@cmedresearch.com<br>Senior Biostat II<br>Cmed (Clinical Research Services) Limited<br>Security Level: Email, Account Authentication (Required) |  <br>Signature Adoption: Drawn on Device<br>Signature ID:<br>C4992A12-1F88-484F-8E7F-8AD1187C30D6<br>Using IP Address: 188.251.30.127<br><br>With Signing Authentication via DocuSign password<br>With Signing Reasons (on each tab):<br>I am the author of this document<br>I am the author of this document | Sent: 12-Jun-2023 \| 17:56<br>Viewed: 12-Jun-2023 \| 17:56<br>Signed: 12-Jun-2023 \| 17:57 |
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