# TRIAL STATISTICAL ANALYSIS PLAN

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| **Document No.:** | c44070053 |
| **BI Trial No.:** | **1502-0001** |
| **Title:** | A Phase I open label study to assess safety, feasibility, efficacy, and biological activity of single administration of Ezabenlimab in combination with BI 765063 and Pembrolizumab in combination with BI 765063 as neoadjuvant treatments in patients with newly diagnosed surgically-resectable, locoregional colorectal cancer |
| **Investigational Product(s):** | Ezabenlimab<br>BI 765063 |
| **Responsible trial statistician(s):** | [redacted]<br>Phone: [redacted] |
| **Date of statistical analysis plan:** | 23 FEB 2024 |
| **Version:** | 1.0 |
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# 1. TABLE OF CONTENTS

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# 2. LIST OF ABBREVIATIONS

| Term | Definition / description |
|---|---|
| BI | Boehringer Ingelheim |
| CTP | Clinical Trial Protocol |
| ECG | Electrocardiogram |
| ICH | International Conference On Harmonisation |
| CTR | Clinical Trial Report |
| PD | Pharmacodynamics |
| PK | Pharmacokinetics |
| SAS® | Statistical Analysis System |
| TSAP | Trial Statistical Analysis Plan |

# 3. INTRODUCTION

As per ICH E9, the purpose of this document is to provide a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and to include detailed procedures for executing the statistical analysis of the primary and secondary variables and other data.

This TSAP assumes familiarity with the Clinical Trial Protocol (CTP). The TSAP readers may consult the CTP for more background information on the study, e.g., on study objectives, study design, population, treatments, definition of measurements and variables, planning of sample size, and randomization.

Due to the early discontinuation of the study following a slow enrolment of only two patients, this TSAP will specify a very limited analysis with data output consisting of a patient profile listing containing data collected for these individual patients.

SAS® Version 9.4 will be used to create the patient profile listing.

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# 4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

Due to the early discontinuation of the study following the enrolment of only two patients, this TSAP will provide only a patient profile listing containing data collected for these individual patients rather than the statistical outputs and analyses described in the trial protocol (including amendments).

The rationale behind creating patient profiles lies in the absence of statistical summary outputs. With a population size of 2, utilizing patient profiles rather than statistical summary outputs will facilitate a more straightforward presentation of the minimal data regarding patient disease background and patient safety details.

# 5. ENDPOINTS(S)

## 5.1 PRIMARY ENDPOINT(S)

The primary endpoints are defined in Section 2.1.2 of CTP. However, due to the early discontinuation of the study following the enrolment of only two patients, only the patient profile listing will be provided in this TSAP.

## 5.2 SECONDARY ENDPOINT(S)

### 5.2.1 Key secondary endpoint(s)

No key secondary endpoint has been specified for this study.

### 5.2.2 Secondary endpoint(s)

The secondary endpoints are defined in Section 2.1.2 of CTP. However, due to the early discontinuation of the study, only the patient profile listing will be provided in this TSAP.

# 6. GENERAL ANALYSIS DEFINITIONS

## 6.1 TREATMENT(S)

For basic study information on investigational products, assignment of treatment, and selection of doses, please see CTP, Sections 3 and 4.

## 6.2 IMPORTANT PROTOCOL DEVIATIONS

Due to the very early discontinuation of the study, any assessed protocol deviations will be provided in the patient profile listing.

## 6.3 INTERCURRENT EVENTS

It is not applicable for this TSAP due to the very early discontinuation of the study.

## 6.4 SUBJECT SETS ANALYSED

Only the treated two patients will be included in the patient profile listing.

[redacted]

## 6.6 HANDLING OF MISSING DATA AND OUTLIERS

Missing or incomplete AE dates are imputed according to BI standards.

## 6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

It is not applicable for this TSAP due to the very early discontinuation of the study.

# 7. PLANNED ANALYSIS

Due to the early discontinuation of the study following a slow enrolment of only two patients, this TSAP will provide a patient profile listing containing data collected for these individual patients rather than the statistical analyses and outputs described in the trial protocol.

## 7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

No descriptive statistics are planned for this section of the report, but the patient profile listing will include the demographics and baseline characteristics data.

## 7.2 CONCOMITANT DISEASES AND MEDICATION

No descriptive statistics are planned for this section of the report, but the patient profile listing will include the concomitant disease and medication data.

## 7.3 TREATMENT COMPLIANCE

This is not applicable for this TSAP due to the very early discontinuation of the study following a slow enrolment of only two patients.

## 7.4 PRIMARY OBJECTIVE ANALYSIS

### 7.4.1 Main analysis

Due to the early discontinuation of the study following a slow enrolment of only two patients, this TSAP will provide a patient profile listing containing data collected for these individual patients rather than the statistical analyses and outputs described in the trial protocol.

[redacted]

### 7.4.4 Supplementary analysis

No supplementary analysis is planned.

## 7.5 SECONDARY OBJECTIVE ANALYSIS

### 7.5.1 Key secondary objective analysis

No key secondary endpoint has been specified for this study.

### 7.5.2 Secondary objective analysis

The secondary objective analysis will not be performed for this study due to its early discontinuation. This TSAP will provide a patient profile listing containing data collected for these individual patients rather than the statistical methods described in the trial protocol.

## 7.6 FURTHER OBJECTIVE ANALYSIS

Further objective analysis will not be performed for this study due to the early discontinuation of the study. This TSAP will provide a patient profile listing containing data collected for these individual patients compared to the statistical methods described in the trial protocol.

## 7.7 EXTENT OF EXPOSURE

It is not applicable for this TSAP due to the very early discontinuation of the study.

## 7.8 SAFETY ANALYSIS

All safety data will be presented in the patient profile listing for two treated patients.

### 7.8.1 Adverse Events

All the adverse events data will be presented in the patient profile listing for two treated patients.

### 7.8.2 Laboratory data

All the laboratory data will be presented in the patient profile listing for two treated patients.

### 7.8.3 Vital signs

The patient profile listing for two treated patients will present the vital signs data.

### 7.8.4 ECG

The patient profile listing will present the ECG data for two treated patients.

## 7.9 OTHER ANALYSIS

No other analyses are planned.

### 7.9.1 Biomarker analyses

It is not applicable for this TSAP due to the very early discontinuation of the study.

### 7.9.2 PK / PD analyses

It is not applicable for this TSAP due to the very early discontinuation of the study.

# 8. TIMEPOINT OF RELEASE OF TREATMENT INFORMATION

As this is an open label study, the treatment information for each patient was loaded into the trial database at trial initiation.

# 9. REFERENCES


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|---|---|
| 9.1 | *BI-VQD-23790-S-G_50-415_AD-02:* “Project Analysis Dataset (PADS) Template (template)”, current version, group / owning department “Med Biostatistics & Data Sciences”, DMS for controlled documents. |
| 9.2 | *CPMP/ICH/363/96:* "Statistical Principles for Clinical Trials", ICH Guideline Topic E9, Note For Guidance on Statistical Principles for Clinical Trials, current version. |
| 9.3 | *BI-VQD-12682-S-G_50-415_AD-03:* “Clinical Trial Analysis Decision Log (template)”, current version, group / owning department “Med Biostatistics & Data Sciences”, DMS for controlled documents. |
| 9.4 | *BI-VQD-12177_40-106_AD-03:* “Clinical Trial Protocol general template for Phase I-IV”, current version, group / owning department “Med Clinical Development & Operations”, DMS for controlled documents. |
| 9.5 | *001-MCS-80-60*6: “Management of Non-Compliances, Audit and Inspection Responses”, current version, group / owning department “Med Quality Medicine”, DMS for controlled documents. |
| 9.6 | *BI-VQD-12045_40-413:* “Identify and Manage Important Protocol Deviations (iPD)”, current version, group / owning department “Med Clinical Development & Operations”, DMS for controlled documents. |
| 9.7 | REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, European Commission webpage. |
| 9.8 | *CPMP/ICH/137/95*: “Structure and Content of Clinical Study Reports”, ICH Guideline Topic E3; Note For Guidance on Structure and Content of Clinical Study Reports, current version, EMA webpage. |
| 9.9 | *001-MCS-30-475_RD-01*: “Biomarker: Intended Use & Implementation Statement (IUIS) (template)”, current version, group / owning department “Med Translational Medicine Clinical Pharmacology”, DMS for controlled documents. |

# 11. HISTORY TABLE

Table 11: 1 History table

| Version | Date (DD-MMM-YY) | Author | Sections changed | Brief description of change |
|---|---|---|---|---|
| 1.0 | **22-FEB-24** | [redacted] | None | This is the final TSAP. |