Statistical Analysis Plan

BerGenBio AS

Protocol: BGBC003

EUDRACT: 2014-000165-46

Investigational Product: BGB324

An open label, multicentre, phase Ib/II study of BGB324 administered as a single agent or in combination with cytarabine or decitabine in patients with acute myeloid leukemia or as a single agent in patients with myelodysplastic syndrome

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Abbreviations

AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AML	Acute myeloid leukemia
APTT	Activated Partial Thromboplastin Time
Ara-C	Cytosine arabinoside
AST	Aspartate Aminotransferase
BM	Bone marrow
BP	Blood Pressure
bpm	Beats per minute
BUN	Blood Urea Nitrogen
°C	Celsius
cm	centimeter
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DLT	Dose limiting toxicity
ECG	Electrocardiogram
EFS	Event Free Survival
ECOG	Eastern Cooperative Oncology Group
HR	Heart rate
INR	International Normalized Ratio
IWG	International Working Group
kg	Kilogram
Max	Maximum
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MDS	Myelodysplastic Syndrome
MedDRA	Medical Dictionary for Regulatory Activities
mmHg	millimeter of mercury
Min	Minimum
MTD	Maximum tolerated dose
NCI	National Cancer Institute
ORR	Objective response rate
OS	Overall survival
PBMC	Peripheral blood mononuclear cells
PK	Pharmacokinetic
PT	Prothrombin Time
RBC	Red Blood Cells
RFS	Relapse Free Survival
RP2D	Recommended Phase II Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SMC	Safety Monitoring Committee
TEAE	Treatment-Emergent Adverse Event

WHO	World Health Organization
WBC	White Blood Cells

1 Introduction

This document presents the statistical analysis plan (SAP) for BerGenBio AS, Protocol No. BGBC003 study submitted in four countries:

- Germany: A Phase Ib/II multicenter open-label study of BGB324(bemcentinib) as a single agent and in combination with cytarabine or decitabine in patients with Acute Myeloid Leukemia (AML) or as a single agent in patients with myelodysplastic syndrome. Final protocol dated 04AUG2020 (Version 10.0).
- Norway: A Phase Ib/II multicenter open-label study of bemcentinib (BGB324) as a single agent and in combination with cytarabine or decitabine in patients with acute myeloid leukemia (AML) or as a single agent in patients with myelodysplastic syndrome (MDS). Final protocol dated 04AUG2020 (Version 8.0).
- United States: An open label, multicentre, phase I/Ib/II study of BGB324 (bemcentinib) administered as a single agent or in combination with cytarabine or decitabine in patients with acute myeloid leukemia (AML) or as a single agent in patients with myelodysplastic syndrome (MDS). Final protocol dated 04SEP2020 (Version 9.0)
- Italy: An open label, multicentre, phase Ib/II study of BGB324(bemcentinib) administered as a single agent or in combination with cytarabine or decitabine in patients with acute myeloid leukemia or as a single agent in patients with myelodysplastic syndrome. Final protocol dated 23MAR2020 (Version 4.0)

The SAP provides the description of the final analyses for all 4 protocols listed above. The data will be analysed together as a unique single study taken into account the individuality of each protocol.

2 Study Objectives

2.1 Primary objectives

The primary objectives of this study are:

Part A:

- In Norway: To identify the maximum tolerated dose (MTD) and/or Recommande Phase 2 dose (RP2D) of BGB324 (bemcentinib) in patients with relapsed or refractory AML or high risk MDS patients.
- In US and Italy: To identify the maximum tolerated dose (MTD) of bemcentinib in AML patients who have received previous treatment with cytotoxic chemotherapy (with or without hematopoietic stem cell transplantation) or a targeted or biologic agent (e.g. hypomethylating agent, tyrosine kinase inhibitor, antibody), and have relapsed after or have been refractory to treatment with such prior therapy.
- In Germany: To identify the maximum tolerated dose (MTD) of bemcentinib in AML patients who have received previous treatment with cytotoxic chemotherapy (with or without hematopoietic stem cell transplantation) or a gene expression modulator, such as a demethylating agent, and have relapsed after or have been refractory to treatment with that therapy.

Part B:

- To identify the safety and tolerability of bemcentinib, as a single agent in patients with AML (Part B1) or MDS (Part B2) and in combination with low dose cytarabine (Part B2 and Part B5) or decitabine (Part B3),
    - In Norway, US and Germany: in patients with AML who are unsuitable for intensive chemotherapy as a result of advanced age or existing co-morbidities.
    - In Italy: in patients with AML who are unsuitable for intensive chemotherapy.

2.2 Secondary objectives

The secondary objectives of this study are:

Part A:

- To identify the dose limiting toxicity (DLT) profile of bemcentinib
- To explore the safety, tolerability and efficacy of bemcentinib
- To characterise the pharmacokinetic (PK) profile of bemcentinib

Part B:

- To explore the efficacy of bemcentinib as a single agent in patients with AML or MDS (part B1 and B4)
- To explore the efficacy of bemcentinib in combination with low dose cytarabine (Part B2 and Part B5) or decitabine (Part B3) in patients with AML who are unsuitable for intensive chemotherapy as a result of advanced age or existing co-morbidities or not.
- To evaluate bemcentinib PK (all Part B cohorts)

2.3 Exploratory objectives

The exploratory objectives of this study are:

- To identify and evaluate potential predictive biomarkers, e.g. soluble AXL (sAXL) and other associated soluble biomarkers. Pre-treatment levels of biomarkers will be correlated with clinical endpoints
- To establish the effects of bemcentinib on relevant biological endpoints in peripheral blood (including sAXL peripheral blood mononuclear cells [PBMC]) and BM samples
- To assess pharmacodynamic biomarkers in tissue and blood to support the clinical development of bemcentinib
- To evaluate other biomarkers relevant to the investigational agents for exploratory purposes

3 Endpoints

3.1 Safety endpoints

Safety and tolerability will be assessed by conducting the following safety assessments at pre-defined time-points during the study:

- Treatment emergent adverse events (TEAE)
- Physical examination

- Vital signs including blood pressure (BP), heart rate (HR), respiration rate and temperature
- Electrocardiogram (ECG)
- Echocardiogram
- Laboratory findings including clinical chemistry, hematology and urinalysis

3.2 Efficacy endpoints

In AML, efficacy endpoints will be measured using objective response criteria, in evaluable patients.

- Objective Response (OR) or Stable Disease (SD) according to the revised recommendations of the International Working Group (IWG) in AML [Cheson, BGBC003 v8.0 (NO); 04 August 2020 CONFIDENTIAL Page 37 of 113 2003 and Döhner, 2017] (see Appendix 5 of the protocol). SD is defined as having unchanged disease for at least 3 treatment cycles.
- Proportion of patients with an OR + SD as an estimate of clinical benefit.
- Relapse Free Survival
- Event Free Survival
- Overall Survival
- To explore the correlation between baseline biomarker levels and clinical endpoints

In MDS, efficacy endpoints will be measured using the following response criteria.

- OR or SD according to the revised recommendations of the IWG in MDS (see Appendix 6 of the protocol). SD is defined as failure to achieve at least PR but not evidence of PD for at least 3 treatment cycles.
- Proportion of patients with an OR + SD as an estimate of clinical benefit.
- Relapse Free Survival
- Event Free Survival
- Overall Survival
- To explore the correlation between baseline biomarker levels and clinical endpoints

3.3 Pharmacokinetic endpoints

Pharmacokinetic analysis is not part of this SAP, it will be summarized in a separate document.

3.4 Pharmacodynamic endpoints

Pharmacodynamic analysis is not part of this SAP, it will be summarized in a separate document.

4 Study Design

4.1 Discussion of Study Design

This is the general summary of the study design in the 4 protocols, detailed design can be found in the individual study protocol for each of the 4 countries.

The design is a Phase Ib/II, open-label, dose-escalation and cohort expansion study to obtain a preliminary assessment of the safety, tolerability and efficacy of bemcentinib, a small molecule inhibitor of Axl kinase in patients with acute AML or high/intermediate (int-2) risk MDS. The study will be conducted at up to approximately 20 sites in Europe and the US and will be performed in approximately 102 evaluable patients with AML or MDS. Additional countries and sites may be added as required to meet the enrolment needs of the study.

Bemcentinib will be administered orally according to a daily schedule during continuous 21-day treatment cycles. During Cycle 1, Week 1 ONLY the first 3 doses of bemcentinib may serve as a 'loading' dose.

Dosing will consist of a loading dose of 200 mg administered on Days 1, 2 and 3 followed by a daily maintenance dose of 100 mg. This dose may be escalated as agreed by the SMC to a maximum daily loading dose of 400 mg on Days 1, 2 and 3 followed by a maximum daily maintenance dose of 200 mg.

Patients will be instructed to take bemcentinib on an empty stomach at a similar time each morning when they wake, or more than 2 hours after a light meal, with water. To maintain a fasted state, patients should be told not eat or drink anything other than water for at least 1 hour after taking the drug.

In Part A the study will follow a 3+3 design to explore the safety and tolerability of repeat dosing of bemcentinib, and to identify the MTD and/or RP2D. A minimum of 6-10 patients will be treated at the MTD and/or RP2D, as determined by the SMC. Depending upon the results of this phase of the study, the safety and efficacy of bemcentinib may be established in up to 4 disease-specific cohorts in Part B.

Part B1

Single agent bemcentinib will be administered to patients with AML who are unsuitable for intensive chemotherapy as a result of advanced age and or existing co-morbidities. In order to be eligible patients should have received at least one line of previous therapy.

Part B2

Bemcentinib will be administered in combination with cytarabine to patients with AML who are not suitable for intensive chemotherapy as a result of advanced age or existing co-morbidities.

Part B3

Bemcentinib will be administered in combination with decitabine to patients with AML who are not suitable for intensive chemotherapy as a result of advanced age or existing co-morbidities.

Part B4

Single agent bemcentinib will be administered to patients with intermediate (int-2) or high risk MDS according to the International Prognostic Scoring System (IPSS) Risk Stratification [Greenberg, 1997]. Patients must have received at least 1 prior treatment for their disease.

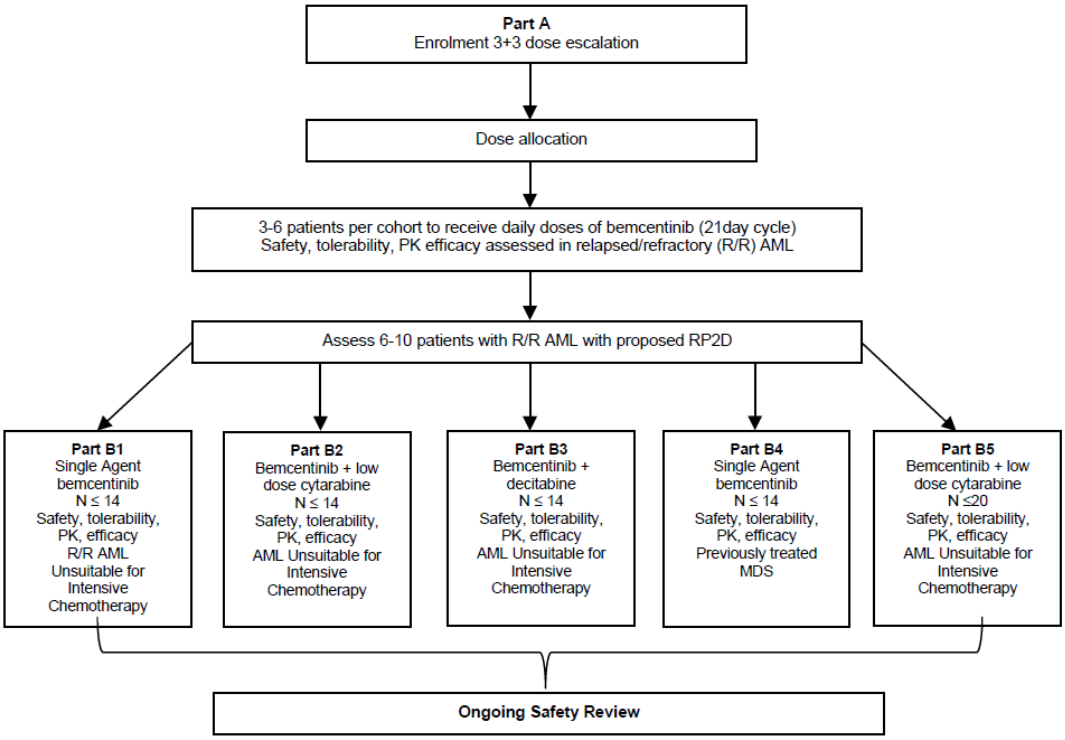
Prior treatment may include those patients who have received hypomethylating agents, decitabine or other approved treatments for MDS.

Part B5

Bemcentinib will be administered in combination with cytarabine in patients with AML who are unsuitable for intensive chemotherapy as a result of advanced age or existing co-

morbidities. Patients must have received at least one prior treatment for AML. Please refer to Figure 1 for an outline of the overall study design.

Figure 1: BGBC003 Study Design



Phase I DLT Assessment Period

During the dose-escalation phase (Part A), safety, tolerability, PK, and preliminary clinical activity of BGB324 will be assessed, and the MTD established, in patients with AML who have received previous treatment with cytotoxic chemotherapy or a targeted or biologic agent (e.g. hypomethyllating agent, tyrosine kinase inhibitor, antibody) or a gene expression modulator, such as a demethylating agent and have relapsed after or have been refractory to treatment with such prior therapy or in high risk MDS. Patients suitable for intensive chemotherapy should be in second or subsequent relapse or be refractory to at least two induction regimens. Patients receiving an allograft in first remission would be eligible at the time of relapse.

A loading dose (Cohort 1) of 200 mg administered on Cycle 1, Days 1, 2 and 3 followed by a daily maintenance dose of 100 mg during continuous 21-day treatment cycles will be evaluated. This dose may be escalated as agreed by the SMC to a maximum daily loading dose of 400 mg on Days 1, 2 and 3 followed by a maximum daily maintenance dose of 200 mg. At least three evaluable patients will be entered per cohort.(see Section 9 of the individuals protocols). At least three evaluable patients will be entered per cohort.

Dose Escalation Scheme

Initially three patients will be recruited into Cohort 1 and will complete 1 cycle of treatment before a dose-escalation evaluation is made. A patient must receive all loading doses and miss no more than 3 standard doses in Cycle 1 in order to be considered as informative to support dose escalation, unless the missed doses are due to bemcentinib toxicity.

The decision to dose-escalate (or not) will be made by the SMC comprising a representative from each actively recruiting investigational site and a representative of the BerGenBio AS study team. Minutes of the SMC meeting will be recorded and circulated for final approval before being placed in the Trial Master File (TMF). The decision to dose escalate will be based upon the tolerability of bemcentinib observed at the previous dose level. Dose escalation will range between 25% and 50% of the previous dose according to the nature and severity of the toxicity observed.

Where dose escalation occurs, three patients will be recruited to the next Cohort (dose level) and will complete 1 cycle of treatment before a dose-escalation evaluation is made, as outlined above.

If one patient in a cohort experiences a DLT during Cycle 1, the cohort will be expanded to six patients. If two of three or two of six patients in a cohort experience DLT no further dose-escalation will take place and the dose below will be nominated as the MTD. If the starting dose exceeds the MTD, a lower dose may be explored if recommended by the SMC. Provided treatment with the starting dose is considered safe by the SMC according to DLT evaluation, dose escalation may proceed.

The maximum daily dose that may be explored in this study will be 400 mg.

If a patient withdraws or is withdrawn for reasons other than DLT prior to completing Cycle 1, the patient will be replaced for the purposes of toxicity evaluation.

Dose Limiting Toxicity

DLT will be assessed during the first 3 weeks of treatment (Cycle 1) with bemcentinib, according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4, considered unrelated to leukemia progression or intercurrent illness, and defined as any of the following:

- CTCAE Grade 3 or 4 nausea, vomiting, or diarrhea that persists despite maximum prophylactic and supportive care
- Any other CTCAE Grade 3 or 4 non-hematological toxicity that is considered to be clinically significant and causally related to BGB324, excluding isolated changes in laboratory results if no clinical significance or no clinical sequelae and adequately improve within 7 days.
- Prolonged neutropenia with ANC < 500 and platelet count < 75000 after Day 42 from the start of treatment in the absence of residual leukemia
- Treatment discontinuation, inability to administer one or more BGB324 loading dose, or inability to administer three BGB324 maintenance doses as result of BGB324-related toxicity
- Any Ventricular Arrhythmia

Part B: Following SMC review of all treatment emergent safety and efficacy data from Part A, up to 14 evaluable patients (up to 20 evaluable patients in Part B5) will be recruited into four cohorts .

Depending upon the safety profile of BGB324 observed in Part A the initial starting dose in combination with cytarabine (Part B2) or decitabine (Part B3), may be reduced by a single dose level (i.e. MTD -1) which will be evaluated in at least three subjects before introduction of the MTD or RP2D identified in Part A. The bemcentinib dose level to be investigated in Part B2 and Part B3 will be dependent upon the MTD confirmed in Part A. A dose lower than 100 mg daily is not available. The Part B5 dose is based on the combination dose that was identified as safe and well tolerated in Part B2.

4.2 Study Treatment

Every patient enrolled in the study will receive bemcentinib. Patients enrolled in Part B2 and B5 will receive bemcentinib in combination with low dose cytarabine. Patients enrolled in Part B3 will receive bemcentinib in combination with decitabine. More detailed information for the treatment scheduled and administration are provided in section 12.1 of the individual protocols.

4.2.1 Bemcentinib

In Part A, the starting dose of bemcentinib (Cohort 1) will be 200 mg on Cycle 1, Days 1, 2 and 3 (loading dose), followed by a daily maintenance dose of 100 mg. In Part B depending upon the safety profile of bemcentinib observed in Part A the initial starting dose in combination with cytarabine (Part B2) or decitabine (Part B3) may be reduced by a single dose level (i.e. MTD -1) which will be evaluated in at least three patients in each cohort before the introduction of the MTD identified in Part A. The bemcentinib dose level to be investigated in Parts B2 and B3 will be dependent upon the MTD confirmed in Part A. A dose lower than 100 mg daily is not available.

The bemcentinib dose in Part B5 (combination with low dose cytarabine) will be 400 mg orally daily for the first 3 days of treatment (loading dose) and 200 mg orally daily thereafter (maintenance dose).

Patients receiving Formulation 2 will be instructed to take bemcentinib on an empty stomach at a similar time each morning when they wake, or more than 2 hours after a light meal, with water. To maintain a fasted state patients should be told not eat or drink anything other than water for at least 1 hour after taking the drug.

Patients will record their dosing at home in a dosing diary that will be reviewed regularly by the site staff. Patients will be instructed as to the importance of following the dosing instructions they have been provided with, and for maintaining an accurate and up to date dosing record. Patients will also be instructed to bring their dosing diary and all bemcentinib bottles, including unused and empty bottles, with them to each study visit. The site staff will record the amount of used and unused bemcentinib capsules at selected study visits.

4.2.2 Cytarabine (Part B2 and Part B5)

For Part B2, cytarabine will be administered subcutaneously according to standard practice (i.e. 20 mg/m2 twice daily for 10 days followed by a rest period of <1 month according to persisting myelosuppression). Cytarabine should be administered approximately 30 minutes after the bemcentinib dose.

For Part B5, cytarabine will be administered at a dose of 20 mg subcutaneously twice daily for 10 days every 28 days. Cytarabine should be administered approximately 30 minutes after the bemcentinib dose.

If toxicity presents, then the cytarabine dose may be modified in accordance with the approved prescribing information or Summary of Product Characteristics (SmPC) and in accordance with local treatment guidelines.

4.2.3 Decitabine

Decitabine will be administered per standard local practice up to a maximum dose of 20 mg/m2 body surface area by intravenous infusion over one hour, repeated daily for five consecutive days (i.e. a total of five doses per treatment cycle).

The total daily dose must not exceed 20 mg/m2 and the total dose per treatment cycle must not exceed 100 mg/m2. The cycle should be repeated every four weeks depending on the patient's clinical response and observed toxicity. Decitabine should be administered within approximately 30 minutes of bemcentinib dose.

If toxicity presents, then the dose may be modified in accordance with the approved prescribing information or SmPC and in accordance with local treatment guidelines.

Both cytarabine and decitabine are considered to be standard of care for these patients and will not be supplied or reimbursed by BerGenBio ASA.

4.3 Study Schedule

The study period will consist of screening, treatment, Final Study Visit, and follow-up. The Final Study Visit will occur 28 days after the patient has discontinued study treatment. A detailed Schedule of Events can be found in the section 9.3 of the Norway, US and German study protocols and 9.2 of the Italian study protocol.

4.3.1 Screening

Patient eligibility for the study will be determined within 14 days prior to the first dose of BGB324. Screening assessment will be conducted according to the schedule of events in section 11 of the protocol.

4.3.2 Treatment

Eligible patients will visit the study site to receive study treatment and protocol-specified procedures according to the relevant Schedule of Events in the study protocol, Section 11. The treatment period will consist of continuous 21-day treatment cycles.

Patients will be intensively monitored throughout Day 1 to Day 4 inclusive of Cycle 1, and in addition will attend the clinic on Day 8, and Day 15.

Patients will attend the clinic once per week during Cycle 2 and then once per cycle thereafter. All patients will continue to receive bemcentinib or the combination for as long as, in the opinion of the investigator, they continue to derive clinical benefit. When there is unacceptable toxicity, confirmed disease progression in the absence of clinical benefit, death or withdrawal of consent, bemcentinib or combination treatment must be discontinued.

For patients in the combination arms (Part B2, B3 or B5), if treatment-related toxicity requires discontinuation, and the toxicity can be clearly assigned to one of the study treatments, the other study drug in the combination can be continued if it is safe to do so (investigator discretion) in the absence of disease progression or intolerable toxicity. The investigator may also decide to discontinue both study treatments at this time.

Patients with AML who are receiving bemcentinib monotherapy and who do not achieve an objective response after two cycles of treatment may start additional therapy with oral anti-metabolites (e.g. 6-mercaptopurine, hydroxyurea), or low dose cytarabine, or melphalan

administered at 50% of the institution's starting dose, which may be escalated in subsequent cycles according to tolerability.

4.3.3 Final Study Visit

Patients will return to the study site for the Final Study Visit 28 days after permanent discontinuation of all study treatments.

4.3.4 Follow Up

An AE will be monitored for 28 days after the last dose of BGB324, although only events considered to be related to treatment need to be recorded in the electronic Case Report Form (eCRF) between the last administration of BGB324 and the end of the 28 day follow up period. If BGB324-related toxicities continue beyond the follow up period, patients will be followed until all BGB324-related toxicities have resolved to ≤Grade 1, stabilised or returned to baseline. If necessary, follow up monitoring for AEs may be conducted over the telephone.

SAEs with a suspected relationship to BGB324 will be collected beyond the 28-day follow-up period until the event is resolved to ≤ Grade 1, stabilized or returned to baseline.

All patients that have permanently discontinued study treatment for whatever reason must be followed for survival. The investigator or designee must confirm with the patient at the time of the Final Study Visit how the patient will be followed for survival (e.g. contact with family or health care provider). Survival follow-up must be conducted at least every 3 months by the investigator or designee and the date-of-death reported in the eCRF.

All subsequent anticancer therapy for AML or MDS must be reported in the eCRF.

4.3.5 End of Study

Except in the case of early termination (Section 9.4), the end of the study is defined as the date when all patients have an OS event, unless the Sponsor terminates OS follow-up once all patients have discontinued study treatment. Should the last patient enrolled to the study be continuing to receive bemcentinib 52 weeks from their Cycle 1 Day 1, the Sponsor may choose to lock the data base to that point and prepare the clinical study report (CSR). Data collected as part of this study after this point, will be reported as an addendum to the CSR.

A final clinical study report will be prepared when the last patient has completed their Final Study Visit and the database is locked. The Statistical Analysis Plan (SAP) will be finalized and signed before database lock.

Patients will continue to be followed for suspected SAEs until these are resolved to ≤ Grade 1, stabilized or returned to baseline. Refer to Section 15.2.2 for SAE reporting after the end of study.

4.4 Concomitant Medication and Procedures

All prescription, non-prescription, or over-the-counter medications including herbal remedies given to, or taken by, the patient at entry and during the study must be clearly documented in the eCRF.

The patients must be instructed that no additional medication will be allowed without the prior consent of the investigator. Any medication considered necessary for the patient's safety and well-being may be given at the discretion of the investigator. Hematopoietic growth factors may be administered for the treatment of AEs such as neutropenic infections but should not be used to maintain the dose intensity of bemcentinib in Part A. Patients who have evidence of treatment benefit after >1 cycle of treatment in Part B may receive hematopoietic growth factors to maintain bemcentinib dosing.

Concurrent treatment with any agent known to cause QT prolongation and have a risk for Torsades de pointes is an exclusion criterion for the study. A comprehensive list of these prohibited medications is provided in the study protocol Appendix 3.
Treatment with any medication which is predominantly metabolized by CYP3A4 and has a narrow therapeutic index is also excluded (see Appendix 4 in study protocol for details of CYP3A4 substrates). Patients being treated with antacid histamine receptor 2 inhibitors or proton pump inhibitors within 3 days of administration of bemcentinib will be excluded. The Investigator may initiate rescue treatment with these medications in the evening for symptomatic relief following one week's treatment with bemcentinib.

4.5 Study Analysis Populations

4.5.1 Enrolled Population

The Enrolled Population will include all patients who have signed the ICF and enrolled into the study (Enrolment date being defined as the date of the first protocol-defined screening procedure).

4.5.2 Safety Analysis Population

The Safety analysis population will be defined as all enrolled patients who receive at least one dose of bemcentinib. The Safety analysis population will be analysed by dose group or combination in Part B.

Patients enrolled to Part A who meet the eligibility criteria for Part B1 and who receive the MTD and/or RP2D, may contribute to the Part B1 analysis.

4.5.3 Efficacy Analysis Population

The Efficacy Analysis Population will include all from Safety Analysis Population that,

- ✓ Meet key eligibility criteria, have assessable disease at baseline and have at least one post-baseline response assessment
- ✓ Have received >1 dose of bemcentinib (and combination agent in Part B2, B3 and B5)

Any patient who continues treatment with bemcentinib beyond confirmed disease progression will be followed for the same safety and efficacy assessments as for all other patients enrolled into the study until they are withdrawn from the study as defined in protocol section 13.

4.5.1 Per protocol Analysis Population

No per protocol population will be analysed in this study.

4.6 Withdrawn Subjects

Patients may withdraw informed consent and discontinue from the study at any time, or for any reason, without prejudice to their future treatment. In addition, a patient must be discontinued from the study if any of the following criteria are met:

- Patient non-compliance with the protocol, as agreed by the investigator and the sponsor
- Patient lost to follow-up
- Termination of the study by the sponsor
- Patient experiences an unacceptable toxicity that precludes them from continuing in the study e.g. patient experiences a ventricular arrhythmia (see study protocol Section 12.2), as agreed by the investigator and the sponsor

- Lack of adequate recovery from a DLT, see Section 9.2.1.2 in study protocol
- Failure of toxicity to adequately resolve, as outlined in Section 12.2 in study protocol
- Female patient becomes pregnant
- Patient experiences clinical disease progression
- Patient and/or investigator decision

AEs resulting in discontinuation will be followed as outlined in study protocol Section 9.3.4.

Patients who discontinue during the DLT assessment period (Part A), for any reason other than a DLT, will be replaced. All other patients who discontinue study treatment will not be replaced.

If a patient discontinues treatment prior to study completion, and for reasons other than progression or non-tolerability, every effort should be made to conduct the Final Study Visit assessments as outlined in Section 11.5 of the protocol. The reason for the patient's withdrawal from the study must be recorded in the eCRF.

4.7 Randomisation

This is a non-randomized study. All patients will receive treatment with orally administered BGB324. All patients enrolled in Part B2 will also receive intravenously administered cytarabine and patients enrolled in Part B3 will receive decitabine in addition to BGB324.

4.8 Blinding

This is an open-label study and consequently there are no blinding procedures in operation.

4.9 Sample Size

Part A of the study follows a conventional algorithm (3+3 patients per dose level) to identify the MTD, escalating on 0/3 or 1/6 patients experiencing a DLT. Under this design, there is a 71% chance of escalation if the true but unknown rate of DLT is 20%, and <50% chance of escalation if the true but unknown rate of DLT is >30%. The operating characteristics of this 3+3 design are outlined in Table 1.

Table 1: Operating Characteristics of the 3+3 Study Design

True but Unknown Rate of DLT (%)	Probability of Escalation (%)
20	71
30	49
40	31
50	17
60	8

The total sample size of Part A depends upon whether DLT(s) is experienced at a given dose level (i.e. whether 3 or 6 patients have been treated) and how many dose levels are tested in order to reach the MTD. A minimum of 6-10 patients will be treated at the MTD.

The sample size of up to 14 evaluable patients for Parts B1, B2, B3 and B4 and up to 20 evaluable patients in Part B5 in this study has been calculated on the basis of the following assumptions for a one-sided, within-group test of proportions, comparing an anticipated ORR of >20% against the null hypothesis rate of 5%, with power 80% for a test of size 0.2. This

calculation is based on statistical significance at the 0.2 level, since this will be taken as evidence of a trend worthy of further study. Although this is offered as a formal sample size calculation, it is acknowledged that for this early-stage study the analyses will be exploratory in nature, and that no account has been taken of multiplicity inherent in the assessment of several, presumably non-independent criteria, for ORR.

5 Statistical Methodology

5.1 Planned Analyses

Disposition analyses will be carried out using the Enrolled Population. Demographic and baseline characteristics analyses will be carried out using the Safety Analysis Set. Safety analyses will be carried out using the Safety Analysis Set. Efficacy analyses will be carried out using the Efficacy Analysis Population.

Summary statistics will be presented for continuous variables, by way of n, mean, standard deviation (SD), median, minimum (Min) and maximum (Max) and by way of group frequencies and percentages for categories of categorical variables. No statistical comparison of dose levels or treatment groups will be performed. Percentages will be calculated using the total patients per dose cohort in the given population unless otherwise noted.

All data from this study will be presented in data listings. All listings will be sorted by dose level or treatment group and patient.

Baseline will be defined as the last assessment prior to study drug administration. Typically this will be Cycle 1 Day 1. Where calculated, absolute change from baseline will be presented using the following formula for each parameter: Value at the visit/timepoint – value at baseline.

Data will be presented by dose/cohort and overall in Part A and by treatment group (AML (B1: BGB324 400/200 mg Single agent; B2: BGB324 400/200 mg + Cytarabine; B3: BGB324 400/200 mg + Decitabine; B5: BGB324 400/200 mg + Cytarabine) and MDS (B4: BGB324 400/200 mg)) and overall in Part B.

Where appropriate, the data for patients who received the MTD during Part A will be combined with that for patients who received the MTD in Part B for the purpose of data summarisation. A clear distinction will be made in the relevant Tables to differentiate between the cohort who received the MTD during the dose escalation phase of Part A, the MTD cohort from the cohort expansion phase in Part A, and the combined MTD cohort.

Any patient treated with bemcentinib beyond disease progression will be followed for the same safety and efficacy assessments as for all other patients enrolled into the study. The data for patients treated beyond progression will be presented in both a combined output (with all patients) and a separate output (reflecting a new period of analysis with the data collected in this period). All data collected will be included in the study CSR and may be presented at congress/symposia.

For subjects in Part B a new period (treated beyond disease progression) will be created if the date of progression < date of any intake of the bemcentinib, to identify patient treated with bemcentinib beyond disease progression and also the visit cycle where the data are collected beyond the disease progression. The data collected during this period will be identified to be added in this analysis.

For Part B analysis, some outputs such as disposition, demographic and baseline characteristics, cancer history, ORR, AE and ECG(QtCF), the data for cohort B2 and B5 will be summarized together.

5.2 Interim Analysis

No formal statistical interim analyses are planned, however data will be monitored by the Safety Monitoring Committee (SMC), in an on-going manner, to assess patient safety.

5.3 Disposition of Subjects

The number of patients receiving study treatment in each analysis population and the reasons for any discontinuation from the study will be presented.

5.4 Baseline and Demographic Characteristics

All baseline and demographic characteristics will be summarised. This will include age, age group, sex, height, weight, and Eastern Cooperative Oncology Group (ECOG) performance status at screening. Cancer history (time since initial diagnosis, type of cancer), medical history by system organ class and preferred term, and prior cancer therapies (chemotherapy, hormonal therapy, immunotherapy, monoclonal therapy, radiotherapy, other therapy) will also be summarized.

The following parameters may be used for defining and comparing the various subtypes of AML patients:

- Age Groups are defined as: <75 years and ≥=75 years of age.
- AML Disease status: Relapsed and Refractory.
- AML Disease Type: Primary and Secondary
- AML Disease Cytogenetic profile: Favorable, Intermediate, Adverse and Not Done

Medical history will be coded according to Medical Dictionary for Regulatory Activities (MdDRA) version 17.0 or higher.

5.5 Concomitant Medication

Medications taken on or after date of informed consent are collected. Prior medications are those that started and stopped before exposure to study medication; concomitant medications are all medications taken during the study period, including those started before but ongoing at first dose.

Incidence of concomitant medication will be presented by therapeutic area and preferred drug name. Prior medications will be listed only.

Where a medication start date is partially or fully missing, and it is unclear as to whether the medication is prior or concomitant, it will be assumed that it is concomitant. Medications will be coded using WHO Drug Dictionary, Mar 2014 or higher.

5.6 Exposure and Compliance

BGB324 exposure will be summarized by the number of cycles started on BGB324 and duration of administration by dose cohort. Duration of BGB324 administration will be defined in days as:

(Date of Last Drug Administration – Date of First Drug Administration + 1 day).

Duration of BGB324 administration will also be summarized in weeks and defined as:

Duration of administration (in days) / 7

Total treatment exposure to BGB324 will also be characterized by total cumulative dose over the whole study and summarized by dose cohort.

For subjects in part B2, total administrations of cytarabine will be summarized by the number of cycles started, the total number of infusions (total number of days cytarabine has been administered), and total cumulative dose administered over the study. The same analysis will be performed for decitabine (part B3).

Study drug percent compliance for BGB324 will be calculated as:

((Actual Duration) / Expected number of doses) * 100

Actual Duration is the sum of each treatment duration by cycle when Dose is not missing or null.

Expected Number of Doses is defined as duration of study drug administration in days (number of cycles received * 21 days).

Overall percent compliance will be summarized by frequency count and percentage of subjects with compliance <80%, 80 to 100%, and > 120%. Overall percent compliance will also be summarized as a continuous variable using descriptive statistics.

Number and percentage of dose reductions per cycle and overall will also be tabulated for part A and Part B.

Number and percentage of dose interruptions per cycle and overall will also be tabulated for part A and Part B. Duration of dose interruptions will also be summarised.

5.7 Efficacy Analysis

The endpoints to be analysed in the efficacy analysis are:

Objective response rate [ORR] : Proportion of patients with a best objective response such as, CR (Complete Remission), Cri (Complete Remission with Incomplete hematologic Recovery), CRp (Complete Remission with Incomplete Platelet Recovery), CRh and PR(Partial Remission) for AML patients and CR, PR, MR(Marrow Response), PMR(Partial Marrow Response) for MDS patients;

CRh is defined as, CR (<5% myelobasts and 0% blasts in the peripheral blood) with partial hematologic recovery, defined as meeting CR criteria but with ANC > 0.5 10^9/L and platelets > 50 10^9/L responses for patients with AML.

Best Objective Response (BOR) = Best response obtain during the study participation for a patient;

Disease control Rate (Objective Response + SD) [DCR]: Proportion of patients with a best objective response such as, CR, CRi, CRp, CRh and PR for AML patients and CR, PR, MR, PMR for MDS patients, + SD (stable disease) as an estimate of clinical benefit;

The ORR will be summarized by;

- Age group (<75 years, >= 75);
- AML Disease Cytogenetic Profile (Favourable, Intermediate, Adverse and not done);

Relapse Free Survival [RFS]

Relapse free survival [RFS]: defined as the months from the date of response until the date of relapse as confirmed by blast counts assessment (date of the disease progression will be used since disease progression is based in blast count assessment) .

Relapse Free Survival is defined only for subjects with a best objective response of CR/CRi/CRp/PR for AML patients or CR, PR, MR, PMR for MDS patients. Subjects who do not achieve CR/CRi/CRp/PR will be excluded from this analysis.

Duration of RFS is calculated as (days):

- Date of disease relapse, patient death, or censoring - Date of first Response evaluation + 1.
- Subjects without an objective disease relapse who die for any reason will be considered to have an event on the date of death. Otherwise subjects will be censored at the date of last objective response assessment showing no relapse has occurred.

Reason for censoring	**Rule**
Early death	Date of death
Disease progression leading to discontinuation	Date of last OR with no relapse
New anticancer treatment started before documentation of disease progression or death	Date of last radiological assessment prior to the start of non-protocol anticancer treatment

RFS will be summarized with (Mean (SD), median, min and max).

RFS will be presented graphically using Kaplan-Meier method.

Event Free Survival [EFS]

Event is defined as death or progression.

Duration of EFS is calculated as (days):

- Date of onset of Event, patient death or censoring - Date of first intake of study treatment (BGB324) + 1.

Situation	**Date of Progression or Censoring**	**Outcome**
New anticancer treatment started before documentation of disease progression or death	Date of last radiological assessment prior to the start of non-protocol anticancer treatment	Censored
Alive and without documentation of disease progression	Date of last radiological assessment	Censored

EFS will be summarized with (Mean (SD), median, min and max).

EFS will be presented graphically using Kaplan-Meier method.

Overall Survival [OS]:

OS is defined as the months from the first day of treatment until date of death for any cause. Patients who were alive at the time of the final analysis will be censored at the date the patients was known to be alive.

Patient who do not die during the study will be followed up until date of death collected in the Survival Follow up CRF form or will be censored with the last Date of Follow-up when the patient was still alive.

Date of last known to be alive is the last date with available information for a subject in the study.

Duration of OS is calculated as (days):

- Date of death or censoring (date of last known to be alive) - Date of first intake of study treatment (BGB324) + 1.

OS will be summarized using Kaplan-Meier estimates (number of subjects who died, number of subjects censored, min, max, median, 95%CI of median).

5.8 Safety Analysis

No formal statistical analysis will be performed. The safety endpoints will consist of treatment-emergent adverse events, physical examinations, vital signs, ECOG, ECG, Echocardiograms, and laboratory tests (clinical chemistry, hematology and urinalysis). Change from baseline will be presented where appropriate.

5.8.1 Adverse events

The number and percentage of patients reporting TEAEs will be tabulated by MedDRA preferred term and system organ class, and summarized by CTCAE grade also. All AEs commencing prior to dosing with study medication will be excluded from the tabulation but will be fully listed.

A subject with more than one occurrence of the same adverse event in a particular system organ class will be counted only once in the total of those experiencing adverse events in that particular system organ class. If a subject experiences the same adverse event at more than one severity, or with more than one relationship to study drug, the most severe rating or the stronger causal relationship to study drug will be given precedence. Any missing severity, causality, or outcome will not be imputed and classed as unknown.

An overall summary classifying subjects with events according to seriousness, severity, maximum relationship to BGB324, and maximum CTCAE grade will also be presented.

Related events are defined as events that are definitely, possibly or probably related to study medication or with an unknown relationship.

Treatment-Emergent AEs are any AEs that start or worsen after first dose of study drug until 28 days following the last dose. AEs with partial onset dates will be assumed to have the latest possible onset date (while accounting for stop date) for determining treatment emergence, but no formal imputation will be done. AEs that have missing onset dates will be considered to be treatment-emergent, unless the stop date is known to be prior to the first administration of BGB324.

5.8.1.1 Subsets

- Non-serious adverse events will be presented by dose level (part A) or treatment group (parts B), system organ class and preferred term

- Related (BGB324) adverse events will be presented by dose level or treatment group, system organ class and preferred term.
- Related (Cytarabine) adverse events will be presented by system organ class and preferred term. (Part B2 only)
- Related (Decitabine) adverse events will be presented by system organ class and preferred term. (Part B3 only)
- Related (Other Anti-Cancer Medications) adverse events will be presented by dose level or treatment group, system organ class and preferred term.
- Serious adverse events will be presented by dose level or treatment group, system organ class and preferred term
- Related (BGB324) serious adverse events will be presented by dose level or treatment group, system organ class and preferred term.
    - Related (Cytarabine) serious adverse events will be presented by system organ class and preferred term. (Part B2 only)
    - Related (Decitabine) serious adverse events will be presented by system organ class and preferred term. (Part B3 only)
    - Related (Other Anti-Cancer Medications) serious adverse events will be presented by dose level or treatment group, system organ class and preferred term.
    - Serious adverse events will be presented by dose level or treatment group, system organ class, preferred term, and maximum CTCAE grade.
- Adverse events leading to discontinuation will be presented by dose level or treatment group, system organ class and preferred term.
- Adverse events ≥ Grade 3 will be presented by dose level or treatment group, system organ class and preferred term.
    - Related (BGB324) adverse events ≥ Grade 3 will be presented by dose level or treatment group, system organ class and preferred term.
    - Related (Cytarabine) adverse events ≥ Grade 3 will be presented by system organ class and preferred term. (Part B2 only)
    - Related (Decitabine) adverse events ≥ Grade 3 will be presented by system organ class and preferred term. (Part B3 only)
- The most frequent MedDRA preferred terms (≥10% subjects in the overall safety population restricted to each part) will be presented by dose level or treatment group.
- Separate listings will be produced for DLTs, SAEs, related (all 3 types) AEs, discontinuations due to AEs, and events of ≥ Grade 3 severity.
- A listing of death occurring during the study with time interval between first/last intake date and death date, as well as a flag for only Early Death during the first 4-week period after C1D1will also be presented.

All other information collected (e.g. action taken) will be listed as appropriate.

Notes:

- AEs coded using MedDRA version 17.0 or higher

5.8.2 Physical Examination

Any new or worsened post-baseline physical examination findings during the safety evaluation period will be recorded as AEs and summarized in terms of AEs as described in Section 5.8.1. Both the complete physical examination performed at screening and the symptom directed physical examination results will be presented in data listings.

5.8.3 Vital Signs

Results for weight (kg), systolic and diastolic blood pressure (mmHg), pulse rate (BPM), respiration rate (BREATHS/MIN), and temperature (°C) will be summarised by dose cohort and scheduled visit, as well as Change from Baseline. Height (cm) at screening will be summarized with the demographics, but presented with other vital signs in the listing.

5.8.4 Eastern Cooperative Oncology Group

ECOG performance status will be summarized categorically at each scheduled visit with frequencies and percentage.

5.8.5 Electrocardiograms

The quantitative ECG assessments (PR interval, RR interval, QRS Duration, QT interval, and QTcF interval) will be summarised for actual values and Change from Baseline to each visit/timepoint will be also presented.

ECG overall interpretation (normal, abnormal not clinically significant and abnormal clinically significant) will be presented as a categorical summary by dose cohort and scheduled visit.

5.8.6 Echocardiograms

Any new or worsened post-baseline echocardiogram findings during the safety evaluation period will be recorded as AEs and summarized in terms of AEs as described in Section 5.8.1. All echocardiogram results will be presented in a data listing.

5.8.7 Laboratory findings

Results from the following laboratory parameters, recorded at scheduled visits, will be presented in listings:

Hematology:

Hemoglobin, Hematocrit, Red Blood Cells (RBC), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), White Blood Cells (WBC), Neutrophils, Eosinophils, Basophils, Lymphocytes, Monocytes, Platelets, and Blasts (in percent).

Clinical Chemistry:

Sodium, Potassium, Calcium, Chloride, Magnesium, Inorganic Phosphate, Creatine phosphokinase, Serum Creatinine, CK-Myocardial B, Total Protein, Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, Albumin, Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Glucose, Uric Acid, and Blood Urea Nitrogen (BUN).

Urine:

pH, Specific Gravity; semi-quantitative "dipstick" evaluation of Proteins, Glucose, Ketones, Blood, Bilirubin, Nitrite, Leukocytes, and Urobilinogen, and a microscopic examination including Casts, Crystals, RBC, and WBC.

Coagulation:

Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), International Normalized Ratio (INR), and Quick Test.

Numeric Hematology and Clinical Chemistry parameters will be summarised along with each corresponding Change from Baseline for all scheduled visit by dose level or treatment group. The incidence of laboratory test results outside the normal range will be listed by dose cohort and time point.

The following shift tables from baseline to all the cycles of hematology CTCAE grades will also be displayed by dose level or treatment group:

- All post baseline grades according to all baseline grades
- Number of patients with at least CTCAE Grade 2 according to all baseline grades

Finally, number of patients with at least CTCAE Grade 3 at each visit will be summarized.

Clinically significant treatment-emergent laboratory findings will be summarised as adverse events.

Notes:

- All results outside predefined normal ranges will be flagged in the data listings.
- Repeat laboratory results within a visit will not be used in any summary calculations. Unscheduled and repeat results will be listed only
- Serum Pregnancy Test results will be listed.
- Any other laboratory results will be listed only.

5.9 Pharmacokinetic Analysis

The Pharmacokinetic Analysis will be conducted separate from this analysis. Details will be found in a specific analysis plan.

5.10 Pharmacodynamic Analysis

The Pharmacodynamic Analysis will be conducted separate from this analysis. Details will be found in a specific analysis plan.

5.11 Protocol Deviations

Deviations from the protocol will be documented on an ongoing basis by the study monitors and project manager throughout the study period.

At the time of database lock, while the protocol deviations are being reviewed, the project manager will forward all relevant documentation highlighting protocol deviations to the study

statistician. These deviations will be included in the protocol violation document for agreement and will be listed with the protocol violations in the CSR.

5.12 Missing Values – Missing Visits

Missing, unused and spurious data will be considered missing at random and dealt with as such. There is no intention to implement any procedure for replacing missing data.

In case of missing or partially missing dates for initial diagnosis, the following rules will be applied:

- If initial diagnosis date=../mmm/yyyy (= missing day), then it will be substituted by **01/mmm/yyyy**
- If initial diagnosis date=.../.../yyyy (= missing day and month), then it will be substituted by **01/JAN/yyyy**
- If initial diagnosis date=.../.../…. (= completely missing), then it won't be substituted.

5.13 Deviations from SAP

Any deviations from the statistical plan will be described and justified in the final clinical study report.

5.14 Changes in Conduct or Planned Analyses from the Protocol

Following are the changes in analyses from those defined in the protocol:

- Population of analysis is updated to match with the usual definition in clinical trials. In the protocol, safety population and efficacy population have the same definition and per protocol population definition is the typically definition of efficacy population. Then, the efficacy population is updated with definition of per protocol and it is decided that no per protocol analysis will be handled.
- The exploratory objective "To explore the correlation between baseline biomarker levels and clinical endpoints". Biomarker data will be analyzed in exploratory analyses not in scope of this SAP so this analysis will be presented within biomarker analysis.

5.15 Algorithms/SAS Codes

- **Tables that need 95% CIs within group for binomial proportions:**
  PROC FREQ DATA=dset;
  BY byvar; (optional)
  TABLES var1/binomial (exact p=.05) alpha=0.05;
  EXACT BINOMIAL;
  RUN;
- **Tables that need life table with estimates of survival, with CIs:**
  PROC LIFETEST DATA=dset OUTSURV=LIFE METHOD=KM;
  BY treatment;
  *TIME duration*censor (0 or 1);*
  RUN;

6 Tables and Listings

6.1 Table Format

All output will be produced using SAS version 9.2 or a later version.

In the top left portion of each table/listing, a *table/listing number* followed by the *title* of the table/listing will be presented. After the title line, optional *sub-title* or *population* information can be presented. Horizontal lines will appear before and after the column heading of the table/listing. *Footnotes* will be put under the main body of text at the bottom of the page.

The *sponsor name*, *protocol number,* programmers User ID, status of the table/listing (i.e. draft or final) and *SAS program name* will appear bottom left in a string and the *page number* will appear on the bottom right corner of each table/listing. The *date and time of creation* of table/listing will appear bottom left under the sponsor name. The source listing number will appear bottom left.

A *landscape layout* is proposed for both table and listing presentations.

The *left* and *right margins* of all tables and listings will be a minimum of 2.1 cm from the left and 1.9cm from the right. The *top and bottom margins* will be a minimum 2.92cm. *Header and footer* will be both 1.27 cm.

There is no special requirement of *font type* and *size*, but an *8-point* font size for tables and *7*or *8-point* for listings is proposed using *Courier New* font. A maximum SAS line size=141 and page size=44 for *8-point* font size, and line size=161 and page size=50 for *7-point* will be used so as to fit on both UK and US paper sizes.

In a listing, in the case that a subject's record has been continued to the next page, an appropriate identification (e.g., the subject ID number) must be presented at the beginning of that page.

6.2 Conventions

Unless otherwise specified, in summary tables of continuous variables, the minimum and maximum values will be displayed to the same number of decimal places as the raw data, the mean and median will be presented to one extra decimal place compared to the raw data, and the standard deviation will be displayed to two extra decimal places compared to the raw data. Wherever possible data will be decimal aligned.

Unless otherwise specified frequency tabulations will be presented by number and percentage, where the percentage is presented in parenthesis to 1 decimal place.

P-values, if applicable, will be presented to 3 decimal places. If a p-value is less than 0.05 but is greater than or equal to 0.01, then an asterisk (*) will be added next to this value. If a p-value is less than 0.01 but is greater than or equal to 0.001, then two asterisks (**) will be added next to this value. Finally, if the p-value is less than 0.001 then three asterisks (***) will be added next to this value and it will be presented as <0.001. If the rounded result is a value of 1.000, it will be displayed as >0.999. Any date information in the listing will use the *date9.* format, for example, 07MAY2002. In the listing, a unit associated with a variable will be presented only once within parentheses either below or next to that variable in the heading portion. If a parameter has multiple units, each unit will be displayed only once, as applicable.

All tables will have their source listing referenced in a footnote. Listings should be sorted by dose level or treatment group, subject and visit and have the source data received by data

management referenced in a footnote. All tables and listings will be converted into Microsoft Word documents and collated into two complete documents.

6.3 Tables

6.3.1 Section 14.1: Demographic and baseline

Table 14.1.1.1	Subject Disposition – Part A (Enrolled Population)
Table 14.1.1.2	Subject Disposition – Part B (Enrolled Population)
Table 14.1.1.3	Important Protocol Violations – Part A (Enrolled Population)
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6.3.2 Section 14.2: Efficacy Analysis

Table 14.2.1.1	Objective Response Rate – Part A (Efficacy Population)
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Table 14.2.2.1	Relapse Free Survival – Summary – Part B (Efficacy Population)
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Table 14.2.4.1	Overall Survival – Kaplan Meier Analysis – Part B (Efficacy Population)

Table 14.2.5.1.1	Objective Response Rate by Age Group – Part A (Efficacy Population)
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Table 14.2.5.1.3	Objective Response Rate by AML Disease Cytogenetic profile – Part A (Efficacy Population)
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6.3.3 Section 14.3: Safety Analysis

6.3.3.1 Adverse events

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Table 14.3.1.1.2	Summary of Adverse Events – Part B (Safety Population)
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Table 14.3.1.3.2.1	Serious Adverse Events by System Organ Class, Preferred Term, and CTCAE Grade – Part A (Safety Population)
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Table 14.3.1.3.3.1	Serious Adverse Events Related to BGB324 by System Organ Class and Preferred Term – Part A (Safety Population)

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6.3.3.2 Laboratory results

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Table 14.3.5.1.2.1	Hematology Results: Shifts from Baseline to all the cycle by CTCAE Grade – Part A (Safety Population)
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Tables, Listings, and Figures will follow the format of:
BGBC003_SAP_Shells_Version1_Final_06Sep2022.rtf

6.6 References

Cheson BD, Bennett JM, Kopecky KJ, et al., Revised Recommendations of the International Working Group for Diagnosis, Standardisation of Response Criteria, treatment Outcomes and Reporting Standards for Therapeutic Trials in Acute Myeloid Leukemia. J ClinOncol (2003) 21 (24): 4642 – 4649

Cheson BD, Greenberg PL, Bennett JM et al., Clinical Application and Proposal for Modification of the International Working Group (IWG) Response Criteria in Myelodysplasia. Blood (2006) 108 (2): 419 – 425

6.7 Appendix

6.7.1 Definitions of End Points for Clinical Trials in AML by Cheson & all 2003.

Outcome	**Response Category**	**Point of Measurement**	**Definition**
Overall survival	All patients	Entry onto trial	Death from any cause
Relapse-free survival	CR	Leukemia-free state	Disease relapse or patient death from any cause
NOTE. Complete blood counts should be evaluated at least monthly, or more often if clinically indicated, to establish the durability of responses.			
Abbreviations: AML, acute myelogenous leukemia; CR, complete remission.			