REDACTED STATISTICAL ANALYSIS PLAN

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Statistical Analysis Plan

Protocol Number: MOR208C205

A Phase II, Two-Cohort, Open-Label, Multicenter Study to Evaluate the Safety and Preliminary Efficacy of MOR00208 Combined with Idelalisib or Venetoclax in Patients with Relapsed or Refractory CLL/SLL Previously Treated with Bruton's Tyrosine Kinase (BTK) Inhibitor

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STATISTICAL ANALYSIS PLAN 2.0

SIGNATURE PAGE

MorphoSys AG
Semmelweis-Strasse 7
D-82152 Planegg
GERMANY

A Phase II, Two-Cohort, Open-Label, Multicenter Study to Evaluate the Safety and Preliminary Efficacy of MOR00208 Combined with Idelalisib or Venetoclax in Patients with Relapsed or Refractory CLL/SLL Previously Treated with Bruton's Tyrosine Kinase (BTK) Inhibitor

Protocol No: MOR208C205

ADDENDA AS COMPARED TO THE ORIGINAL SAP VERSION 2.0

Analyses that were added to the SAP are depicted in the Table below. No analyses that have been specified in the original SAP Version 2.0 were changed or removed.

SAP Section	Changes	Rationale
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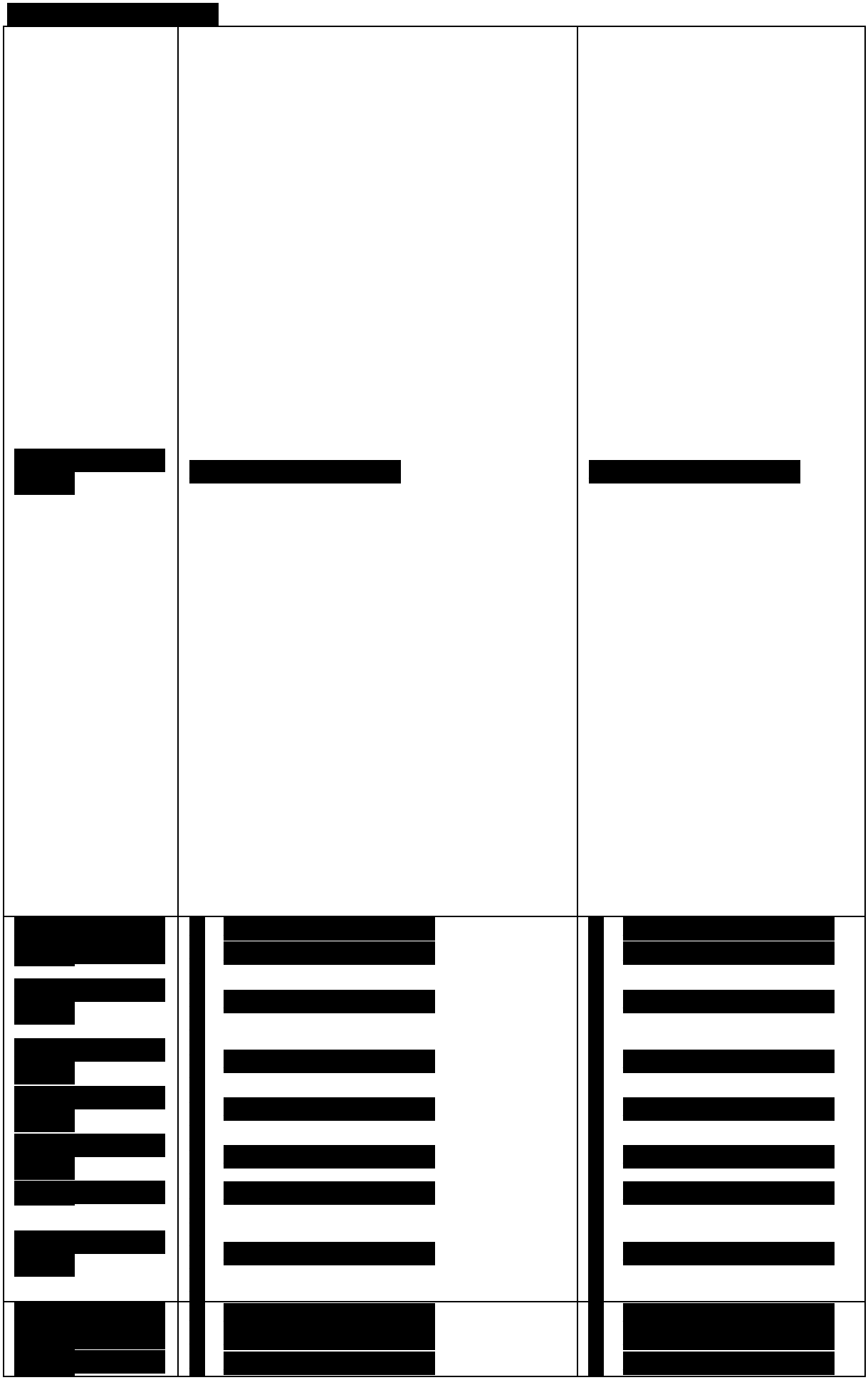

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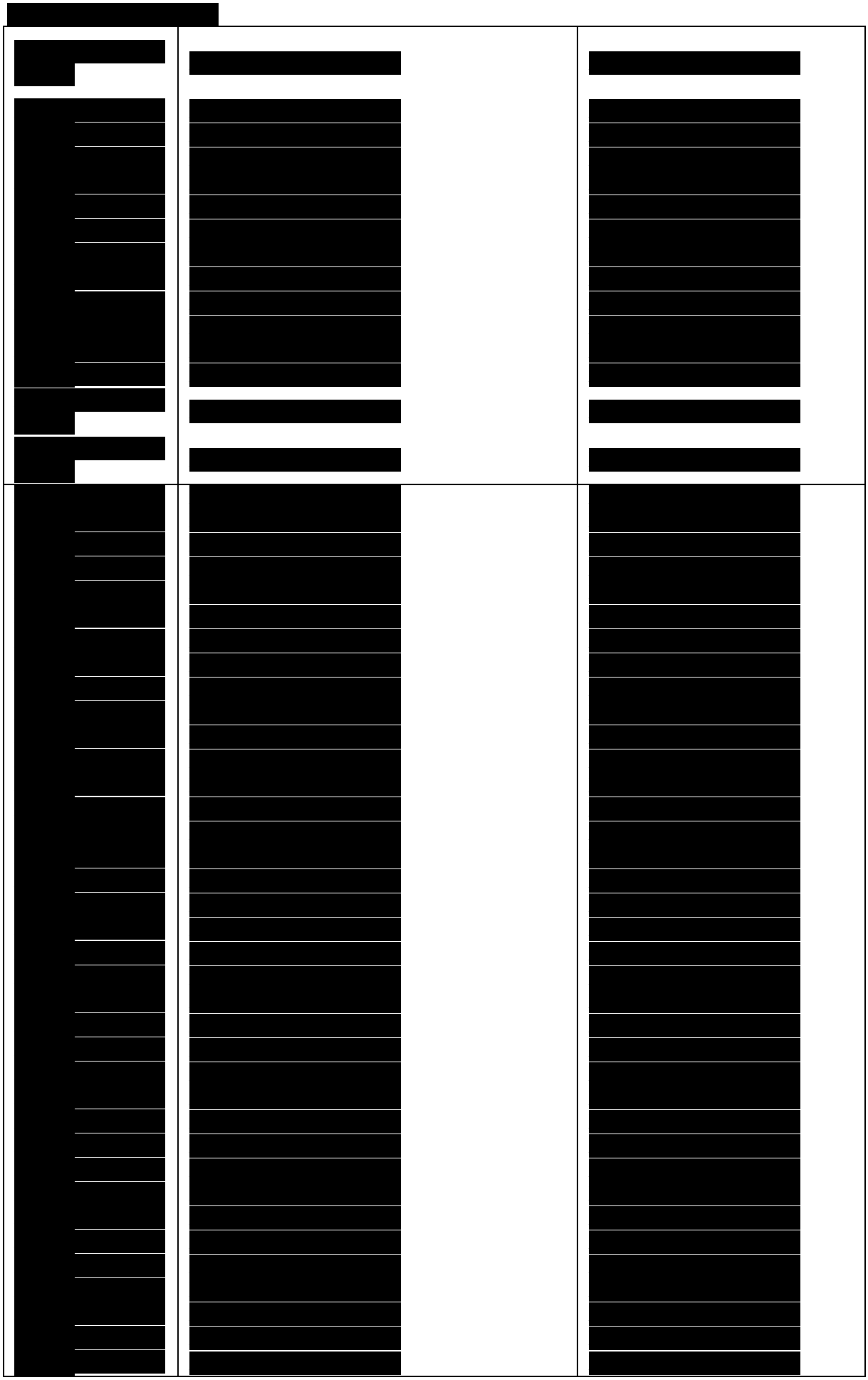

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Contents

List of Tables

(Excluding those in the appendix)

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Abbreviations

ADaM	Analysis dataset model
ADCC	Antibody dependent cell mediated cytotoxicity
ADS	Analysis dataset
AE	Adverse event
AESI	Adverse event of special interest
ALP	Alkaline phosphatase
ALT (SGPT)	Alanine transaminase (serum glutamic pyruvic transaminase)
ANC	Absolute neutrophil count
ANOVA	Analysis of variance
Anti-HBc	Hepatitis B core antibody
AST (SGOT)	Aspartate aminotransferase (serum glutamic oxaloacetic transaminase)
ATC	Anatomical Therapeutic Chemical (classification system)
BID	*bis in diem*, twice daily
BLQ	Below the limit of quantification
BM	Bone marrow
BTK	Bruton's tyrosine kinase
C1D1	Cycle 1 Day 1
CD	Cluster of differentiation
CLL	Chronic lymphocytic leukemia
CMV	Cytomegalovirus
CPMP	Committee for Proprietary Medicinal Products (now: CHMP, Committee for Medicinal Products for Human Use)
CR	Complete response/remission
CRi	Complete response with incomplete marrow recovery
CSR	Clinical Study Report
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of variation
DBP	Diastolic blood pressure
DNA	Deoxyribonucleic acid
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EDTA	Ethylenediaminetetraacetic acid
EMA	European Medicines Agency
EOT	End of Treatment
EudraCT	European Clinical Trials Database
FAS	Full analysis set
FCBP	Females of childbearing potential
FcγR	Fc (fragment crystallizable) gamma receptors
FDA	Food and Drug Administration
FISH	Flourescence in-situ hybridization
GGT	Gamma-glutamyltransferase
HCG	Human chorionic gonadotropin
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HR	Heart rate (pulse rate)
IB	Investigator’s Brochure
IAS	Immunogenicity analysis set
ICF	Informed Consent Form
ICH	International Conference on Harmonization

IDMC	Independent Data Monitoring Committee
Ig	Immunoglobulin
IGHV	Immunoglobulin heavy-chain variable gene
IND	Investigational New Drug application
IRR	Infusion-related reaction
IV	Intravenous(ly)
IWCLL	International Workshop on Chronic Lymphocytic Leukemia
LDH	Lactate dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
MRD	Minimal residual disease
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NE	Not evaluable
NHL	Non-Hodgkin's lymphoma
NK	Natural killer (cells)
o.d.	Once daily
ORR	Overall response rate
PD	1. Pharmacodynamic(s), 2. Progressive disease, 3. Protocol deviation
PDVD	Programming Development and Validation Document
PB	Peripheral Blood
PE	Physical examination
PJP	Pneumocystis jirovecii pneumonia
PK	Pharmacokinetic(s)
PKAS	PK analysis set
PLC	Phospholipase C
PLL	Prolymphocytic leukemia
PPS	Per-protocol set
PR	Partial response/remission
PRL	Partial response with lymphocytosis
PT	Preferred Term
QA	Quality assurance
QC	Quality control
RBC	Red blood cell
RNA	Ribonucleic acid
R/R CLL	Relapsed or refractory chronic lymphocytic leukemia
R/R SLL	Relapsed or refractory small lymphocytic lymphoma
SAE	Serious adverse event
SAF	Safety analysis set
SAP	Statistical Analysis Plan
SAR	Serious adverse reaction
SAS	Statistical Analysis System
SBP	Systolic blood pressure
SD	Stable disease
SDTM	Study data tabulation model
SJS	Stevens-Johnson syndrome
SLL	Small lymphocytic lymphoma
SOC	System Organ Class
SOP	Standard operating procedure
sqrt	Square root
StD	Standard deviation
T-CLL	Chronic lymphocytic leukemia of T-cell type (now: T-cell prolymphocytic leukemia)
TEAE	Treatment-emergent adverse event
TEN	Toxic epidermal necrolysis
TLGO	Tables, Listings, Graphs and other Output
TLS	Tumor lysis syndrome

TP53	Tumor protein p53
UK	United Kingdom
US	United States of America
WBC	White blood cell
WHO	World Health Organization
ZAP-70	Zeta-chain-associated protein kinase 70

1 Related Documents

This document presents the Statistical Analysis Plan (SAP) for MorphoSys AG Protocol No. MOR208C205: A Phase II, Two Cohort, Open-Label, Multicenter Study to evaluate the Safety and Preliminary Efficacy of MOR00208 Combined with Idelalisib or Venetoclax in Patients with Relapsed or Refractory CLL/SLL previously treated with Bruton's Tyrosine Kinase (BTK) Inhibitor.

This SAP is based on the final protocol Amendment No. 6, Version 10.0 dated 25 July 2017.

The SAP provides the description of the final statistical analysis to be reported in the Clinical Study Report (CSR). In case of deviations from the SAP, explanations will be provided in the CSR.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH E9: FDA and CPMP). All work planned and reported from this SAP will follow internationally accepted guidelines for statistical practice, published by the American Statistical Association (ASA 1999) and the Royal Statistical Society (RSS 2014).

The planned analysis identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data and will not require updating the final SAP. Any post-hoc, or unplanned, exploratory analysis performed will be clearly identified as such and described in the final CSR.

The reader of this SAP is encouraged to also read the clinical protocol, and other identified documents, for details on the planned conduct of this study. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

2 Definitions

Cohorts

Statistics will be displayed for the following cohorts, i.e., treatment groups:

- **MOR00208 + Idelalisib (Cohort A)**
- **MOR00208 + Venetoclax (Cohort B)**

The treatment label **"MOR00208 + Idelalisib"** and **"MOR00208 + Venetoclax"** should be displayed in the Tables, Listings, Graphs and other Output (TLGO).

In case that at least one patient has received only one of the treatments of the cohort he/she was enrolled to, in addition to the column containing all patients of the cohort additional columns will be generated containing the actual treatment the patients have received as column header. E.g., if a patient is enrolled into Cohort B but discontinues the study after only one dose of MOR00208 and before the first planned dose of venetoclax then all summaries of safety will also include a column with treatment label **"Treated with MOR00208 only"**, a column with treatment label **"Treated with MOR00208 + Venetoclax "** and a column with treatment label **"Enrolled to MOR00208 + Venetoclax"**. Safety tables for adverse events will further contain two columns **"Overall Combination Treatment"** and **"Overall At Least One Study Drug"**.

Definition of Baseline

Baseline is defined to be the latest non-missing assessment value for a patient, for that particular parameter collected prior to initiation of first dose of either study medication.

Change from baseline value at each post baseline assessment will be calculated as post baseline value – baseline value.

Date of Start of Treatment Period

In general, the date of start of treatment period should coincide with the day one of first study medication intake. However, discrepancies between these dates may arise and the most appropriate date to be used in such situations requires a case-by-case evaluation. Since many algorithms used in the statistical analysis require the start of the treatment period to be identified, an ad-hoc variable specifying this date will be defined. The date of start of treatment period will be initially set equal to the date of first study medication intake for all patients. The need for deviations from this rule in single cases will be evaluated during the data review.

3 Overall Study Design and Plan

3.1 Study Objectives and Endpoints

Objectives and endpoints are identical for both cohorts with one exception regarding the definition of the overall response rate. Details are specified in **Table 1**.

Table 1: Overview of Study Objectives and Endpoints

Study objective	Endpoint	Analysis
Primary objective: • To determine the safety of MOR00208 combined with idelalisib or venetoclax	**Primary endpoint:** • Incidence, frequency and severity of adverse events (AEs)	See section 4.10.1
Secondary objectives: • To determine the quality of the response	**Secondary endpoints:** • Best objective response rate (ORR): o Definition for Cohort A: percentage of patients achieving a complete response (CR), a partial response (PR) or a partial response with lymphocytosis (PRL). o Definition for Cohort B: percentage of patients achieving a CR or a PR.	See section 4.8.1
• To assess the potential immunogenicity of MOR00208 (anti-MOR00208 antibody formation)	• Anti-MOR00208 antibody formation (ADA): number and percentage of patients who develop anti-MOR00208 antibodies; Titer determination; Characterization of ADA-positive samples (neutralizing vs non-neutralizing).	See section 4.9.1
• To assess the pharmacokinetic (PK) profile of MOR00208	• Pharmacokinetic analysis for MOR00208: plasma concentration-time profiles of MOR00208 and appropriate individual PK parameters (e.g., accumulation ratios).	See section 4.9.2

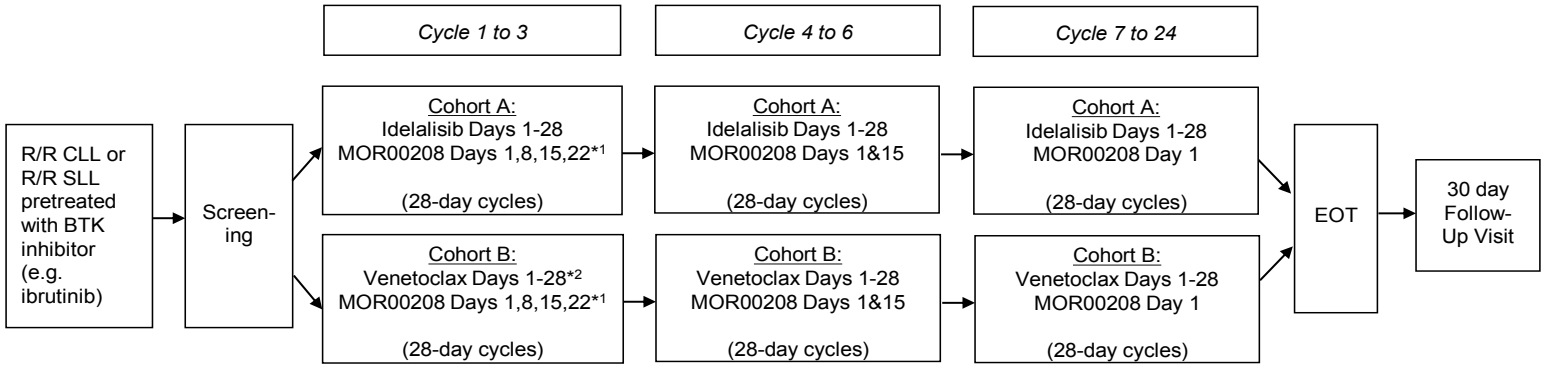
Exploratory objectives: • To assess minimal residual disease (MRD) in patients achieving a complete or partial response	**Exploratory endpoints:** • Proportion of patients with MRD-negativity	See section 4.9.3
• To explore putative predictive biomarkers	• Absolute and percentage change from baseline in measurements for B-, T- and natural killer (NK) cell populations	See section 4.9.4

The exploratory objective "To determine and correlate prognostic factors with efficacy parameters" specified in the protocol was not addressed in the present SAP. Due to several protocol amendments the primary focus of the study has shifted to address safety-relevant questions. Given the small sample size no subgroup analyses could be conducted, which would have been necessary to adequately address the objective.

3.2 Discussion of Study Design

This is a multicenter, two-cohort, open-label phase II study of MOR00208 combined with idelalisib (Cohort A) or venetoclax (Cohort B) for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (R/R CLL) or relapsed or refractory small lymphocytic lymphoma (R/R SLL) pretreated with a BTK inhibitor as a single agent or as part of a combination therapy. Recruitment of a patient into Cohort A or B is at the discretion of the Investigator. A total of 10 to approximately 12 patients are planned to be enrolled in each cohort in Europe and the US. **Figure 1** illustrates the design of the study.

Figure 1: Study Design



*1 Additional loading dose of MOR00208 on Cycle 1 Day 4

*2 Weekly ramp up of Venetoclax starting on Cycle 1 Day 8 (C1D8: 20mg, C1D15: 50mg, C1D22:100mg, C2D1: 200mg). Venetoclax dosis 400mg up from Cycle 2 Day 8

Abbreviations: EOT=end of treatment; BTK=Bruton's tyrosine kinase; R/R CLL=relapsed or refractory chronic lymphocytic leukemia; R/R SLL=relapsed or refractory small lymphocytic lymphoma.

The study will include a safety run-in phase for each cohort enrolling 10- approximately 12 patients per combination treatment. MOR00208 will be administered at a dose of 12.0 mg/kg as intravenous (IV) infusion, idelalisib in Cohort A as 150 mg oral tablets twice daily and venetoclax in Cohort B as 400 mg oral tablets daily dose. To mitigate the risk for tumor lysis syndrome (TLS) treatment of patients with venetoclax will be initiated after an initial treatment with MOR00208 at 20 mg up from C1D8 for 7 days, followed by a weekly ramp-up dosing schedule to the recommended daily dose of 400 mg. The safety run-in phase will be concluded with an evaluation of the safety data of all treated patients once 10 patients completed at least one treatment cycle in Cohort A or at least 5 weeks of combination treatment in Cohort B. The first 3 patients in Cohort A will be dosed sequentially at least 48 hours apart. In Cohort B, all 10- approximately 12 patients will be dosed sequentially, at least one week apart.

In Cohort A there will be two safety evaluations. After completion of the first cycle (4 weeks) the safety data of the first three patients will be evaluated. This evaluation will be done by an Independent Data Monitoring Committee (IDMC) composed of experts in the field of oncology and clinical biostatistics who have no other role in the study and do not have an affiliation with the Investigators or the sponsor. After the evaluation of the safety data from the first 3 patients for Cycle 1 of treatment and a positive recommendation from the IDMC the next 7- approximately 9 patients may be dosed in parallel. An additional IDMC review will take place after 10 patients completed at least 1 cycle of treatment.

In Cohort B the safety evaluation will be performed by the IDMC after the first 10 patients completed at least 5 weeks of combination treatment. The evaluation will be done by the IDMC as already described. Importantly, all patients in Cohort B, who participate in the safety run-in phase, will be hospitalized on the day of the first two dose escalations of venetoclax (C1D8 and C1D15).

The criteria for the evaluation of safety of the combination therapy will be defined by the IDMC and laid down in the Safety Management Plan of the trial.

During the study, MOR00208 will be administered as infusions 12.0 mg/kg in 28-day cycles. From Cycle 1 to 3, each cycle will consist of weekly infusions (on Day 1, Day 8, Day 15 and Day 22). In Cycle 1, an additional loading dose will be administered on Day 4. From Cycle 4 to 6, MOR00208 will be administered on a biweekly basis with infusions on Day 1 and Day 15 of each cycle. Thereafter, MOR00208 will be administered on Day 1 of each cycle starting with Cycle 7 Day 1.

Idelalisib will be self-administered twice daily starting on Day 1 of each cycle. Venetoclax will be self-administered (except during hospitalization) starting from Cycle 1 Day 8 and on Day 1 of each cycle onwards. Treatment with idelalisib or venetoclax may be modified in a de-escalating fashion or discontinued based upon clinical and laboratory findings. In case idelalisib or venetoclax treatment was stopped due to side effects suspected to be related to idelalisib or venetoclax, the patient may continue MOR00208 treatment.

Progressive disease will require discontinuation of study medication.

Patients who benefit from treatment are allowed to continue MOR00208 treatment beyond Cycle 24 at Investigator's discretion. The total duration of the study will be limited to a maximum of 5 years from first patient first visit or up to the timepoint of approximately 30 days after last patient received his last treatment, whichever comes first.

3.3 Study Treatments

3.3.1 Treatment Period

The treatment period consists of a total of 24 cycles, each cycle lasting 28 days.

One to four visits are foreseen for each treatment cycle with one additional loading dose of MOR00208 on Day 4 of Cycle 1. Day 1 is the main visit of each cycle, where the largest number of examinations and assessments will be performed (see **Table 2**). Idelalisib or venetoclax tablets will be handed to the patients on Day 1 of each cycle.

Patients who continue to derive benefit from therapy with MOR00208 can stay on MOR00208-treatment even beyond Cycle 24. In this case, the patient should be followed up at further visits (C25D1, C26D1, etc.) as specified for Cycle 7 to Cycle 24 (see **Table 2**). Examinations which are not performed on every cycle, e.g., radiological and PK examinations, should also be followed up according to the specifications made in Schedule of Assessments. Patients who achieved a confirmed CR or PR with bone marrow MRD negativity are allowed to stop idelalisib or venetoclax treatment and proceed with monthly MOR00208 treatment per discussion between the Investigator and sponsor's medical monitor.

3.3.2 Treatment administration

MOR00208

MOR00208 will be administered IV at a dose of 12.0 mg/kg.

For the first 3 months (3 cycles) of the study, each cycle will consist of a MOR00208 infusion on Day 1, Day 8, Day 15 and Day 22 of the cycle. In addition, a loading dose will be administered on Day 4 of Cycle 1. Thereafter, MOR00208 will be administered on a biweekly basis (every 14 days) with infusions on Days 1 and 15 of each 28-day cycle from Cycle 4 to 6, and on a monthly basis on Day 1 of each cycle from Cycle 7 Day 1.

Idelalisib

The recommended starting dose for idelalisib is 150 mg orally, twice daily (BID). It may be taken with or without food approximately at the same time of the day. Ideally, doses should be taken at ~12-hour intervals (e.g., at ~8 AM and at ~8 PM) on a BID schedule beginning ~30 minutes prior to the initial MOR00208 infusion.

Patients will self-administer the dose of 150 mg twice daily orally continuously during the study duration. Treatment may be continued up to 24 cycles, or until progression of disease, withdrawal of consent, unacceptable toxicity, death or patient is lost to follow-up, whichever occurs first.

Venetoclax

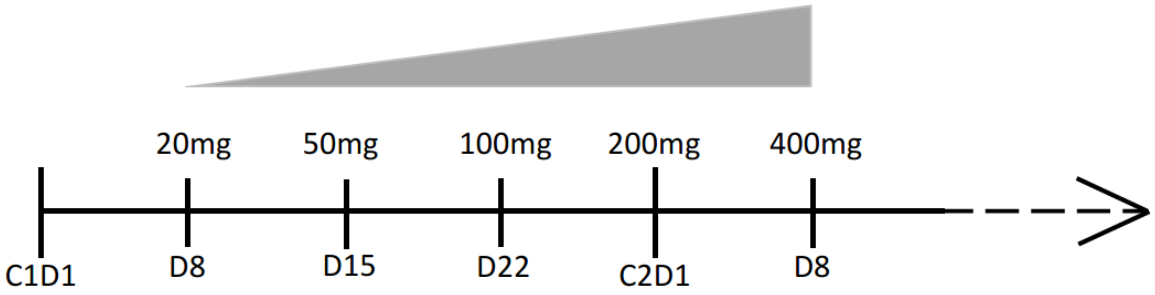
Venetoclax dose should be administered according to a weekly ramp-up schedule over 5 weeks to the recommended daily dose of 400 mg.

Figure 2 illustrates this initial ramp-up. The dosing schedule for ramp-up phase is given as follows, daily dose of venetoclax: 20 mg 1st week of combination treatment, 50 mg 2nd week, 100 mg 3rd week, 200 mg 4th week and 400 mg 5th week and thereafter. The 5-week ramp-up dosing schedule, starting on C1D8, is designed to gradually reduce tumor burden (debulk) and decrease the risk of TLS. Assessment of patient-specific factors for level of risk of TLS and prophylaxis for TLS should be performed prior to first dose of venetoclax (see Section 8.10.1 of the protocol).

Venetoclax should be taken as scheduled orally once daily up to 24 cycles, or until disease progression or unacceptable toxicity is observed. Venetoclax tablets should be taken with a meal and water at approximately the same time each day. Tablets should be swallowed whole and not chewed, crushed, or broken prior to swallowing. If the patient misses a dose within 8 hours of the time it is usually taken, the patient should take the missed dose as soon as possible and resume the normal daily dosing schedule. If a patient misses a dose by more than 8 hours, the patient should not take the missed dose

and should resume the usual dosing schedule the next day. If the patient vomits following dosing, no additional dose should be taken that day. The next prescribed dose should be taken at the usual time.

Figure 2: Ramp-up Dosing Schedule for Venetoclax



3.4 Study Schedule

- Prior to start of any study-related examination the Investigator or designated staff will fully explain the study to potential patients, to obtain their written informed consent.
- The Screening Period begins on the date when the Informed Consent Form (ICF) is signed; it will last for up to 28 days and is followed by Cycle 1 Day 1 (C1D1).
- The treatment period consists of a total of maximum 24 cycles of combination therapy (i.e., MOR00208 and idelalisib/venetoclax), each cycle lasting 28 days. Patients who continue to derive benefit from therapy with MOR00208 can stay on MOR00208-treatment even beyond Cycle 24. Study treatment will continue until documented disease progression, intolerable toxicity, withdrawal of consent to continue study treatment, death, physician decision, or early termination of the study. At that time, an End of Treatment (EOT) visit will be performed.
- Follow-up Period:

  30 Day Safety Follow-up Visit: A safety follow-up visit scheduled 30 days after the last dose of the study treatment to follow up for adverse events (AEs) and serious adverse events (SAEs) that may have occurred after discontinuation from the study treatment regardless of the reason for study drug discontinuation.

  Follow-up for Drug Discontinuation/Patient Withdrawal from Study: If a patient discontinues study treatment and is withdrawn from the study for any reason he/she will attend the EOT visit, if possible, and complete all assessments. In the event that a patient discontinues prematurely from the study due to a treatment-emergent adverse event (TEAE) or serious TEAE, the TEAE or serious TEAE will be followed until it resolves (returns to normal or baseline values) or stabilizes, or until it is judged by the Investigator to be no longer clinically significant.

The study plan and scheduled tests are summarized in **Table 2**.

Table 2: Schedule of Procedures and Assessments

Evaluation or Procedure	Screening Period	Treatment Period												
	Screening ≤28 Days prior to D1	Cycle 1					Cycle 2				Cycle 3			
Day	**Screen**	**D1**	**D4**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**
Informed consent	X													
Inclusion/exclusion criteria	X	X[1]												
Demography	X													
Medical history	X													
Disease staging	X													
Disease risk assessment: Cytogenetic testing; β_2-microglobulin (serum); Expression of CD38 and ZAP-70		X[1]												
Optional mutational analysis (e.g., IGHV, TP53, NOTCH1, BTK, PLCγ2)		X[1]												
Previous/concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete physical examination	X													
Limited physical examination		X			X		X		X		X		X	
ECOG performance status	X	X[1]					X				X			
Weight/height [2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
B symptoms	X	X					X				X			
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead resting ECG	X	X[1]			X[3]		X[3]				X[3]			

Evaluation or Procedure	Screening Period	Treatment Period												
	Screening ≤28 Days prior to D1	Cycle 1					Cycle 2				Cycle 3			
Day	**Screen**	**D1**	**D4**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**
Urinalysis	X	X					X				X			
HIV testing	X													
Serum pregnancy test (FCBP)[4]	X													
Urine pregnancy test [1,4]		X					X				X			
Pregnancy and risks counselling	X													
"Emergency laboratory" [1, 5]		X	X	X	X	X	X	X	X	X	X	X	X	X
Central laboratory (blood) Hematology	X	X[1]			X[1]		X[1]		X[1]		X[1]		X[1]	
Central laboratory (blood) Serum chemistry	X	X[1]			X[1]		X[1]		X[1]		X[1]		X[1]	
Central laboratory (blood) Coagulation	X	X[1]					X[1]				X[1]			
Serology (hepatitis B and C)	X[12]										X[12]			
CMV testing	X[14]						X[14]				X[14]			
B-, T- and NK cell (blood) [1]		X		X			X[17]		X[16]					
CD19 assessment (CD19ABC and % CD19 + cells) (blood) [1]		X		X[16]	X[16]		X[17]							
Anti-MOR00208 antibodies [1]		X					X				X			
Optional FcγR polymorphism (mucosal		X												

Evaluation or Procedure	Screening Period	Treatment Period												
	Screening ≤28 Days prior to D1	Cycle 1					Cycle 2				Cycle 3			
Day	**Screen**	**D1**	**D4**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**	**D1 ±1 day**	**D8 ±1 day**	**D15 ±1 day**	**D22 ±1 day**
cheek swab) [1]														
CD16 assessment (CD16ABC) (blood) [1]		X												
ADCC (blood) [1]		X												
MRD (blood) [1]		X												
Disease response assessment: CT/MRI of neck, chest, abdomen, pelvis [7]	X													
MOR00208 administration		X	X	X	X	X	X	X	X	X	X	X	X	X
Dispensation of idelalisib/venetoclax tablets		X[17]		X[16]	X[16]	X[16]	X	X[16]			X			
Venetoclax ramp-up [18]				20mg	50mg	100mg	200mg	400mg						
TLS risk assessment [1,16,18]	X			X	X	X	X	X						
(S)AE assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PK MOR00208		X[6]	X[6]		X[6]		X[6]		X[6]		X[6]		X[6]	

Schedule of Procedures and Assessments (continued)

	Additional Treatment Periods				**Follow-up Period**
Evaluation or Procedure	**Cycle 4 - Cycle 6**		**Cycle 7 - Cycle 24**	**End of Treatment Visit (EOT)**	**30-Day Safety Follow-up Visit**
Day	**D1 ±2 days**	**D15 ±2 days**	**D1 ±2 days**	**Preferably within ≤30 days of last dose of study treatment**	**±2 days**
Concomitant medication	X	X	X	X	X
Complete physical examination				X	
Limited physical examination	X	X	X		X
ECOG performance status	X		X	X	
Weight [2]	X	X	X	X	
Vital signs	X	X	X	X	
B-symptoms	X		X	X	X
12-lead resting ECG	X		X	X	
Urinalysis	X		X	X	
Serum pregnancy test (FCBP) [4]				X	
Urine pregnancy test [1]	X		X		
Emergency Laboratory [1, 5]	X	X	X		
Central laboratory (blood) Hematology)	X[1]		X[1]	X	
Central laboratory (blood) Serum chemistry	X[1]		X[1]	X	
Central laboratory (blood) Coagulation	X[1]		X[1]	X	
Anti-MOR00208 antibodies	X[1, 9]		X[1, 9]	X	
B, T, and NK cell (blood) [1]		X[10]		X	

	Additional Treatment Periods				**Follow-up Period**
Evaluation or Procedure	**Cycle 4 - Cycle 6**		**Cycle 7 - Cycle 24**	**End of Treatment Visit (EOT)**	**30-Day Safety Follow-up Visit**
Day	**D1 ±2 days**	**D15 ±2 days**	**D1 ±2 days**	**Preferably within ≤30 days of last dose of study treatment**	**±2 days**
Disease response assessment: CT/MRI of neck, chest, abdomen, pelvis [7]	X[7]		X[7]	X[7, 8]	
For CR / PR patients only: bone marrow aspiration & biopsy, MRD assessment	X[11]		X[11]	X[11]	
MOR00208 administration	X	X	X		
Dispensation of idelalisib/venetoclax tablets	X		X		
(S)AE assessment	X	X	X	X	X
CD19 assessment (CD19ABC and % CD19+ cells) (blood)				X	
PK MOR00208	X[1, 9]		X[1, 9]	X	
Antineoplastic therapy after end of study treatment					X
Serology (hepatitis B and C)	X[12]		X[12]		
MRD (blood) [1]	X[13]		X[13]		
CMV testing	X[14]		X[14]		

Abbreviations: ABC=antibodies bound per cell; ADCC=antibody-dependent cell-mediated cytotoxicity; AE=adverse event; β-HCG=beta-human chorionic gonadotropin; BTK=Bruton's tyrosine kinase; CMV=Cytomegalovirus; CD19=cluster of differentiation 19; CT=computed tomography; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; FCBP=female of childbearing potential; HIV=human immunodeficiency virus; IGHV=immunoglobulin heavy-chain variable gene; MRD=minimal residual disease; MRI=magnetic resonance imaging; NK=natural killer; PK=pharmacokinetics; SAE=serious adverse event; TLS=tumor lysis syndrome.

Disease risk assessment as per IWCLL guideline: cytogenetic tests: FISH: Minimum required tests are del (17p), del (11q), del (13q), trisomy 12, karyotyping. IGHV information can be obtained from previous CLL history; should otherwise be obtained from baseline investigation, B_2 microglobulin (serum), CD38 (cytometry), ZAP-70 (cytometry).

[1]Before study drug administration.
[2]Body height will be measured at Cycle 1 Day 1 (C1D1) only. Weight and height should be measured while the patient is without shoes but dressed.
[3]12-lead resting ECG performed 1 hour ±10 minutes post-MOR00208 dosing
[4]Pregnancy tests for FCBP: a serum pregnancy test must be performed at screening within 7 days prior to the start of study drug and a local urine pregnancy test within 24 hours prior to the start of study drug. The results of both tests must be negative in order to receive C1D1 dosing. A β-HCG pregnancy test should also be performed at the EOT visit. At all other indicated timepoints, a urine pregnancy test for FCBP will be performed locally. Pregnancy test must be negative for dosing.
[5]Emergency laboratory sample to be collected and evaluated in the local laboratory as indicated and reviewed by study treating physician before study drug administration.
[6]MOR00208 PK sample will be taken pre-dose and 1 hour ± 10 min after the end of MOR00208 infusion.
[7]Baseline CT/MRI scan has to be performed within 14 days before C1D1. CT scans performed prior to screening as part of the regular clinical work-up of the patient will be allowed up to 6 weeks before C1D1. However, a CT scan must be performed within the 14 day period prior to C1D1 for those patients with signs of rapidly progressing disease at screening. CLL response assessment according to IWCLL guideline (Hallek et al., 2008). SLL response assessment according to the Lugano Classification criteria (Cheson et al., 2014). For CLL and SLL: CTs or MRIs will be performed at C4D1, C7D1, C13D1, C19D1, etc. Time window is ±7 days for visits C4D1 and C7D1 and ±14 days for the following examinations. A CT/MRI scan has to be performed at least 8 weeks after CR was identified by clinical criteria (and before a BM biopsy is obtained for CR confirmation). If a regular CT/MRI scan is scheduled within these 8 weeks according to the schedule of assessment (C4, C7, C13, etc.) this examination should be postponed to meet the confirmation timeline. The following regular CT/MRI scan can be postponed/skipped, if this examination is within 8 weeks of the CR confirmatory scan.
[8]In case the patient is withdrawn from treatment for reasons other than progression of disease, a CT is only required at the EOT visit if this was not performed within 28 days before EOT.
[9]During Cycles 4 through 24, anti-MOR00208 antibody samples and MOR00208 PK samples (all to be collected pre-dose only) will be collected in odd numbered cycles only (i.e., Cycles 5, 7, 9, 11, etc.)
[10]B/T/NK cell count only in Cycle 4 of additional treatment period.

[11]**For patients with CR:** a MRD assessment from bone marrow aspirate and a local analysis of bone marrow aspiration/biopsy has to be performed for confirmation of CR at least 8 weeks after the CR criteria for tumor response are first met. The result of the CT scan need to be obtained first; if this does not confirm a CR, then a biopsy should not be performed.
For patients with PR and PB MRD negativity: an MRD assessment from bone marrow aspirate/peripheral blood has to be performed at least 8 weeks after the PB MRD negativity was detected.
[12]If positive for hepatitis B serology needs to be followed up locally every 2 months.
[13]Periphal blood sample for MRD assessment has to be taken at C4D1, C7D1, C13D1, C19D1, etc. until BM MRD negativity was confirmed.
For CR patients only: An additional PB sample needs to be obtained at the time when CR is confirmed by CT.
[14]Patients with positive serology or with other evidence of a history of CMV infection at screening should be carefully monitored with PCR
(a) monthly, if initial PCR result has been negative without associated clinical signs of CMV infection or
(b) weekly, if significant CMV viremia has been detected.
[15]During ramp-up of venetoclax patients will receive 20 mg (C1D8), 50 mg (C1D15), 100 mg (C1D22), 200 mg (C2D1) and 400 mg (C2D8), if no contraindications
[16]**Cohort B** –Venetoclax+MOR00208 patients only.
[17]**Cohort A** – Idelalisib+MOR00208 patients only.
[18]In cases when an unscheduled visit needs to be performed during ramp-up phase of venetoclax (e.g., due to dosing interruption or reduction of venetoclax which leads to changed treatment schedule of venetoclax), no risk reassessment for TLS needs to be performed at respective regular visit(s) when MOR00208 is administered.

3.5 Concomitant Medication

Patients are allowed to continue the medications that they are taking at baseline. Patients may also receive concomitant medications that are medically indicated as standard care for the treatment of symptoms and intercurrent illnesses. Section 8.13 of the protocol details prohibited concomitant medications.

3.6 Study Analysis Populations

The following analysis populations are defined:

3.6.1 Full Analysis Set (FAS)

The Full analysis set (FAS) will include all patients who receive at least one dose of MOR00208 and/or one dose of idelalisib in Cohort A and/or one dose of 100 mg daily dose of venetoclax in Cohort B. The FAS will be the primary analysis population for the secondary endpoint Overall Response Rate (ORR).

In the FAS patients will be analyzed according to the cohort they were enrolled (intent-to-treat principle).

3.6.2 Per Protocol Set (PPS)

The Per Protocol Set (PPS) consists of all patients in the FAS who did not have any protocol deviations that could confound the interpretation of the efficacy analyses conducted on the FAS. Patients with no post-baseline assessment of response will be excluded from the PPS. The PPS will be used for a sensitivity analysis of the secondary endpoint overall response rate (ORR).

Decisions about whether a protocol deviation is relevant for the exclusion of a patient from the PPS will be made before database closure. In the PPS patients will be analyzed according to the cohort they were enrolled.

3.6.3 Safety Analysis Set (SAF)

The Safety Analysis Set (SAF) includes all patients who received at least one dose of any study treatment and had at least one post-baseline safety evaluation. A record of death or “no adverse event” constitutes a valid safety assessment. Data for patients with no post-baseline safety assessment will only be listed in the FAS. Patients will be analyzed according to the study treatment they actually received. The SAF will be used for the primary endpoint analysis, i.e., incidence and severity of adverse events.

3.6.4 PK Analysis Set (PKAS)

The PK analysis set (PKAS) will include all patients who received at least one dose of study medication MOR00208 and have at least one quantifiable serum MOR00208 concentration. PK parameters will be calculated as data permit.

3.6.5 Immunogenicity Analysis Set (IAS)

The Immunogenicity Analysis Set (IAS) will include all patients who have at least one anti-MOR00208 antibody assessment.

3.6.6 Other Populations Defined for Tables and Listings

Two further populations are defined for the case any additional tables and listings will be presented:

- All patients
- All enrolled patients
- Screening failure patients

The “all patients” population consists of all patients who have signed informed consent. The ‘all enrolled patients’ population includes all patients who received at least one dose of any study treatment.

The following **Table 3** summarizes the analyses being performed for each analysis set.

Table 3: Overview of the Analyses Performed on the Different Study Populations

Analysis	All patients	FAS	PPS	SAF	PKAS	IAS
Patient disposition	**x**	**x**				
Summary of demographic and baseline characteristics		**x**		**x**		
Incidence, frequency and severity of adverse events				**x**		
Summary of vital signs, 12-lead ECG, laboratory safety evaluations				**x**		
ECOG and B-symptoms				x		
Overall response rate		**x**	**x**			
Study treatment (exposure, compliance, dose reductions, dose interruptions)		**x**		**x**		
Summary of prior CLL therapies		**x**		**x**		
Summary of pre-medication, prior medication, concomitant medication, and medical history/current medical conditions		**x**		**x**		
Pharmacokinetic analyses					**x**	
Immunogenicity analyses						**x**
Descriptive biomarker analyses		**x**				

3.7 Withdrawn Patients

Once a patient is withdrawn from the study, the patient may not re-enter the study.

3.8 Randomization

The study is a non-randomized trial.

3.9 Blinding

This is an open label study.

3.10 Sample Size

The primary endpoint of this study is the incidence and severity of AEs in Cohort A (MOR00208 combined with idelalisib) and Cohort B (MOR00208 combined with venetoclax) and will be analyzed

descriptively. In each cohort approximately 12 patients will be enrolled. No formal sample size calculation was performed and no formal statistical hypothesis testing is planned.

4 Statistical Methodology

4.1 General Statistical Approaches

4.1.1 Descriptive Statistics

All data will be summarized using appropriate statistics (counts/percentages for discrete variables, mean, median, standard deviation, minimum, maximum, number of valid observations for continuous variables) for tabulation purposes. For specific variables, 95% confidence limits of means will be presented. The number and percentage of patients in each category will be presented for categorical variables. For categorical variables, the number and percentage of patients with missing data will be provided. Data from all sites will be pooled for all analyses.

4.1.2 Statistical Significance

No formal statistical hypothesis testing is planned.

4.1.3 Subgroup Analyses

No subgroup analyses are planned in the study.

4.1.4 Visit Window

Analysis Window

For parameters that will be summarized by visit, the nominal visit as recorded on the eCRF will be used. There will be no additional analysis windowing done based on the assessment date.

Unscheduled visits prior to C1D1 will be included for the calculation of baseline values.

Unscheduled scans will be used for determination of tumor response efficacy endpoints.

Selection of Data in the Event of Multiple Records in a Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value per visit, whereas a time-to-event analysis would not require 1 value per analysis window but rather 1 value for the study. Unless otherwise noted throughout the rest of this document, when a single value is needed, the following rule(s) will be used:

- If more than 1 assessment occurs during the same nominal visit, select the record closest to the nominal day for that visit.
- If there are 2 assessments that are equidistant from the nominal day, the data of the assessment after the scheduled study day will be used.
- The last measurement will be used if multiple measurements are all taken on the same day.

4.1.5 Exclusion of Data from the Statistical Analysis

No data will be excluded from the analyses, including any outliers.

4.1.6 Listings

All data collected in the CRF will be presented in the listings.

4.2 Types of Planned Analysis

4.2.1 Primary Analysis

The primary analysis of each cohort to evaluate safety and preliminary efficacy will be based on the safety data and response assessment of the enrolled patients up to the time point of 3-18 months after last patient started treatment in Cohort B.

4.2.2 Final Analysis

The final analysis will be conducted at the end of the study defined as 5 years after the first patient was enrolled (C1D1) or approximately 30 days after last patient received his last treatment, whichever comes first.

4.3 Disposition of Patients

The number of patients screened, the number (%) of screen failures and the number of patients with each reason for screen failure will be presented (by cohort). All patients will be included.

The following summaries will be provided by cohort based on the total number of enrolled patients:

- An overview table will be provided by cohort and will include the number of patients enrolled, the number (%) of patients in each analysis set (FAS, PPS, SAF, PKAS and IAS).
- Number (%) of patients who were treated with study drug (split by MOR00208, idelalisib/venetoclax, and treated with both drugs).
- Number (%) of patients who were enrolled but not treated with study drug (split by MOR00208 and idelalisib/venetoclax).
- Number (%) of patients who discontinued treatment including the reason for discontinuation.
- Number (%) of patients who are still on any treatment (only for the primary analysis).The median time on study will be reported for patients in the FAS, which is defined as follows: [(Date of Death/last Visit including the End of Treatment Visit) – (Date of first dosing with any study drug) + 1]/30.4375.

The median time on study will be derived using Kaplan-Meier-Methodology. Patients still on study at data cut-off will be censored.

The individual time on study will be graphically illustrated by a ‘Swimmers Plot’. The graph will indicate the point in time the best response is reached, the best response (complete response vs. partial response), the number of prior treatment lines, and the reason for BTK inhibitor discontinuation in the last BTK inhibitor containing line. Moreover, the point in time MRD negativity is reached will be shown (see Section 4.9.3). For MRD negativity it will be differentiated between blood and bone marrow assessments, i.e., it will be indicated in the ‘Swimmers Plot’ when MRD negativity is reached as assessed in blood vs. bone marrow.

4.4 Baseline and Demographic Characteristics

4.4.1 Demography/Baseline Characteristics

All summaries will be presented overall and by cohort in the FAS and SAF. For categorical variables, the number and percentage of patients with missing data will be provided. Demographic and baseline characteristics will include the following:

- age (both continuous and categorical, i.e., <65 and ≥65, <70 and ≥70)
- sex and race
- height and weight
- ECOG and disease staging (see section 4.4.2)

- number of prior systemic treatment lines
- time since first CLL/SLL diagnosis (i.e., the interval between the date of first CLL/SLL diagnosis and the screening visit; reported in months)
- time on BTK inhibitor treatment (months) in the most recent prior therapy line containing a BTK inhibitor (not necessarily the last line before entering COSMOS). The following terms will be considered to find the last BTK-containing therapy line: 'ibrutinib', 'imbruvica', 'ACP-196', 'acalabrutinib', 'CC-292', 'AVL-292', 'ONO-40-59', 'BGB-3111'. The variable will be derived as follows: [(End of treatment date for the BTK inhibitor) – (Treatment start date for the BTK inhibitor) + 1]/30.4375.
- the number of patients with beta-2 microglobulin levels >3mg/L at baseline (3 mg/L corresponds to 254.45 nmol/L).
- the number of patients with:
    - neutrophil count $\leq 1.5 \times 10^9$ cells/L at baseline
    - hemoglobin ≤11 g/dL at baseline
    - platelet count $\leq 100 \times 10^9$ platelets/L at baseline

The last three items will be summarized for the FAS only. For the time on BTK inhibitor treatment in the most recent prior therapy line containing a BTK inhibitor the following imputations for missing start and stop dates will be made: If the day of the start or stop date is missing but the month is present the day will be imputed by the 15th of the month. If the month of the start or stop date is missing no imputations will be done and the time on BTK inhibitor will be considered as missing.

The demography and baseline characteristics assessed will also be listed by patient.

Note:

- Weight recorded at all the cycles will be presented in the summary of vital signs;
- Baseline BMI will be calculated as: weight at baseline (kg)/squared height at Cycle 1 Day 1 (m^2).

4.4.2 Disease Staging

The "Binet staging system" and "Modified Rai Clinical Stage" for disease staging information collected at baseline will be summarized by cohort.

The Binet clinical staging system and the modified Rai clinical staging system for CLL/SLL comprise three stages (see Section 6.1).

4.4.3 FcγRII/III Gene Mucosal Cheek Swab

Following subgroups will be defined: FcγRIIIa high affinity (FCGR3A-158V homozygosity) vs. FcγRIIIa low affinity (FCGR3A-158F homozygosity, or FCGR3A-158F/V heterozygosity). FcγRIIa high affinity (FCGR2A-131H homozygosity) vs. FcγRIIa low affinity (FCGR2A-131R homozygosity, or FCGR2A-131H/R heterozygosity). The number (%) of patients in each subgroup will be summarized by cohort.

4.4.4 Cytogenetic Risk

Listings and tables for the mutational status of genes such as immunoglobulin heavy-chain variable gene (IGHV), NOTCH1, tumor protein p53 (TP53), BTK, phospholipase C γ2 (PLCγ2) will be presented. The tables will summarize the number and proportion of patients with mutations present in the aforementioned genes.

Similarly, information will be provided for both translocations and deletions associated with prognosis. Genetic lesions or translocations will be determined by *fluorescence in situ hybridization*

(FISH).The number and proportion of patients with abnormal FISH results for the genetic regions 17p13, 11q13, 13q14, 13q34, 14q32, 6q22-q23 will be presented. The number (%) of patients with complex karyotype will be summarized.

Listings will display detailed information on test results for each individual patient.

4.5 Medical History and Current Medical Conditions

Medical History and Current Medical Conditions will be summarized by body system and by toxicity grade for each treatment group. Summaries will be produced using the SAF and FAS.

Notes:

- Toxicity grade will be coded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) V4.03 or higher.
- Medical history is defined as records in the "Medical History and Current Medical Conditions"- eCRF form which are not ongoing at Cycle 1 Day 1.
- Current medical conditions are defined as records in the "Medical History and Current Medical Conditions"- eCRF form which are ongoing at Cycle 1 Day 1.

4.6 Prior and Concomitant Medications and Therapies

Prior medications and concomitant medications will be summarized by cohort for the SAF and FAS using frequency distributions and percentages by Therapeutic Subgroup (2^{nd} level of the Anatomical Therapeutic Chemical [ATC] classification) and Preferred Name.

The medications will be classified according to the following rules:

- Prior medication: start date < date of start of treatment period and stop date ≤ date of start of treatment period
- Concomitant medication: date of start of treatment period ≤ start date < date of study completion/discontinuation
- Prior and Concomitant Medication: start date < date of start of treatment period and stop date > date of start of treatment period or ongoing

The prior and concomitant medications will be listed by Therapeutic Subgroup (2^{nd} level of the ATC classification) and Preferred Name for each patient.

<u>CLL/SLL-specific prior therapies:</u>

The best response and duration of response to the previous regimens patients received will be listed. Duration of Response (DoR) to previous regimens is defined as time (in months) from date of assessment of initial tumor response (CR or PR/PRL) to date of assessment of tumor progression (PD). A partial completion date of initial response and progression will be handled using the algorithm specified in section 4.14.1 (handling of missing data). Furthermore, the time since the completion of last regimen will be listed. Partial completion dates will be imputed using the algorithm specified in section 4.14.1 (handling of missing data).

The number (%) of patients who received 1, 2, 3, etc. prior regimens will be provided. Descriptive statistics will also be provided for the last regimen patients received prior to study entry and the best response (n, %) and duration of response to last therapy (in months). The reason for discontinuation of prior BTK inhibitor will be listed and summarized. The following terms will be used to identify prior BTK inhibitor therapy:

- ibrutinib and imbruvica

- acalabrutinib and ACP-196

- CC-292 and AVL-292

- ONO-40-59
- BGB-3111

Additionally, listings on CLL/SLL-specific surgeries, radiation, and stem cell transplantations will be presented. The number and proportion of patients who have experienced these procedures will be tabulated.

4.7 Study Treatment

All analyses on study treatment will be conducted on the SAF and the FAS.

4.7.1 Duration of Exposure

Exposure to combination treatment (i.e., both MOR00208 and idelalisib or venetoclax) and each individual study drug will be summarized for the FAS and the SAF.

4.7.1.1 Duration of Exposure to Each Individual Study Drug

Duration of exposure to an individual study drug (days) = (last date of exposure to study drug) – (date of first administration of study drug) + 1.
Taking into account the period of rest between infusions, the **last date of exposure** is defined as follows:

- For MOR00208: When the study drug is administered over several regular doses with regular time intervals, the last date of exposure is identified according to the planned dose schedule of the cycle. If no rest period is included in the cycle then the last date of exposure is: (last date of administration of the study drug) + (length of time interval-1). **Length of time interval**: 7 days in Cycle 1-3 and 14 days in Cycle 4-6 a, and 28 days from Cycle 7 onwards.
- For idelalisib and venetoclax, the last date of exposure will be defined as the last date of administration.
- For idelalisib and venetoclax, temporary dose interruptions will not be considered for calculation.

4.7.1.2 Duration of Exposure to Combination Treatment (i.e., the combination of *both* MOR00208 and idelalisib/venetoclax at the same time)

Duration of exposure to combination treatment (days) = (last date of exposure to both MOR00208 and idelalisib/venetoclax) – (date of first administration of study treatment) + 1.
The last date of exposure for each individual drug is specified in *Section 4.7.1.1*.

4.7.1.3 Exposure Analysis

- The number of patients completing each cycle will be summarized and listed. A patient is considered to have completed a cycle for MOR00208 if he/she was compliant for all MOR00208 infusions during the cycle. A patient is considered to have completed a cycle for idelalisib or venetoclax if he/she was compliant for idelalisib or venetoclax administration during the cycle.
- Duration of exposure will be calculated for the following categories: Week (1-2], (2-4], (4-6], (6-8], etc. Summaries (i.e., mean, standard deviation, etc.) will be displayed in weeks.
- Number of infusions with MOR00208 will be summarized.

4.7.2 Dose Reduction

Dose reductions are only possible for venetoclax and idelalisib, but not for MOR00208. The number (%) of patients with any (i.e., permanent and transient) dose reduction will be summarized. For idelalisib, the number (%) of patients with a permanent reduction to 100 mg BID will be summarized. For venetoclax, the number of patient with a *permanent* reduction to 300 mg, 200 mg, or 100 mg will

be summarized. Moreover, the number (%) of patients who underwent no permanent reduction at all will be shown per cohort.

4.7.3 Dose Interruption

The number (%) of patients with temporary interruptions and the associated reasons will be summarized for both study drugs split by cohort.

4.7.4 Treatment Compliance

If the ratio (total used dose)/(total planned dose) is between 80% (exclusive) and 120% (inclusive) of the assigned dosage during a particular Cycle, then the patient is considered compliant for treatment.

The planned dose and the used dose will be calculated based on information collected on the eCRF pages '*Idelalisib Dosing Record'* or *'Venetoclax Dosing Record'*. As patients may change the daily dose, or transiently interrupt treatment, information on dosing will be represented differently in the eCRF for different situations:

- Patients who changed the Actual Total Daily Dose have **two (or more)** eCRF log lines for a particular Cycle or treatment period (during venetoclax ramp-up), i.e., one separate log line for each particular Actual Total Daily Dose. Each eCRF log line will contain information on the number of tablets dispensed, and the number of tablets returned.
- Patients who interrupted treatment and re-initiated treatment in the same Cycle (or same treatment phase during ramp-up) have **two (or more)** eCRF log lines. The Actual Total Daily Dose in each log line will be identical. All eCRF log lines will contain the information on the number of tablets dispensed, and the last log line will contain the information on the number of tablets returned.
- Patients who interrupted treatment, and only re-initiated treatment at the beginning of the next Cycle or next treatment period (during venetoclax ramp-up) will have **one** eCRF log line containing all information on Actual Total Daily Dose, number of tablets dispensed, and number of tablets returned.
- Compliant patients will display only one eCRF log line for a particular cycle, or treatment phase.

The number of days on treatment for a particular Actual Total Daily Dose (represented by an individual eCRF log line) is calculated as follows:

(Dosing Stop Date – Dosing Start Date) + 1.

The number of days on treatment will be derived for every single eCRF log line.

Idelalisib

Idelalisib is dispensed in 28-day Cycles. The administration is bi-daily (100 mg BID or 150 mg BID). Compliance will be calculated based on the total planned dose, and the total dose actually used.

- The total ***planned*** dose per Cycle can be calculated as follows:

  - **For Cycles with one eCRF log line:**
    Actual Total Daily Dose as entered in the eCRF [mg] x Number of days on treatment.

  - **For Cycles with two or more eCRF log lines (two log lines in case of one dose change, or treatment interruption with re-initiation in the same Cycle):**
    E.g., for two log lines:
    (Actual Total Daily Dose as entered in the eCRF [mg] in log line 1 x Number of days on treatment in log line 1) + (Actual Total Daily Dose as entered in the eCRF [mg] in log line 2) x (Number of days on treatment in log line 2).

    Note: Actual Total Daily Dose may be identical for different log lines (in case of interruption), or different in case of dose change.

- The total dose ***used*** per Cycle can be derived as follows:

  - **For Cycles with one eCRF log line:**
    (Actual Total Daily Dose as entered in the eCRF [mg] / 2) x (Number of tablets dispensed – Number of tablets returned).

  - **For Cycles with two or more eCRF log lines:**

    - **All log lines contain information on the number of tablets dispensed, and number of tablets returned (in case of dose change):**
      E.g., for two log lines:
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 1 / 2) x (Number of tablets dispensed in log line 1 – Number of tablets returned in log line 1)] +
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 2 / 2) x (Number of tablets dispensed in log line 2 – Number of tablets returned in log line 2)].

    - **All log lines for a particular Cycle contain the information on the number of tablets dispensed, and only the last log line for a particular Cycle contains number of tablets returned (in case of treatment interruption and re-initiation of treatment in the same Cycle):**
      E.g., for two log lines:
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 1 / 2) x (Number of tablets dispensed in log line 1)] - [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 2 / 2) x (Number of tablets returned in log line 2)].

- Calculation of compliance for a particular Cycle (%):

(sum of total dose *used* for all log lines pertaining to a particular Cycle) / (sum of total *planned* dose for all log lines pertaining to a particular Cycle) * 100.

Venetoclax

The planned daily doses of venetoclax in the ramp-up phase and beyond are as follows:

- 20 mg 1st week (study days 8 to 14)
- 50 mg 2nd week (study days 15 to 21)
- 100 mg 3rd week (study days 22 to 28)
- 200 mg 4th week (study days 29 to 35)
- 400 mg 5th week and thereafter (study days 36 and above)

Different tablet strengths are being used to target a particular Actual Total Daily Dose:

- 20 mg daily: 2 x 10 mg tablet (i.e., 14 tablets for 7 days)
- 50 mg daily: 1 x 50 mg tablet (i.e., 7 tablets for 7 days)
- 100 mg daily: 1 x 100 mg tablet (i.e., 7 tablets for 7 days)
- 200 mg daily: 2 x 100 mg tablet (i.e., 14 tablets for 7 days)
- 300 mg daily: 3 x 100 mg tablet (i.e., 84 tablets for 28 days)
- 400 mg daily: 4 x 100 mg tablet (i.e., 112 tablets for 28 days, or 84 tablets for 21 days)

For an Actual Total Daily Dose beyond 100 mg, only tablets of strength 100 mg are being administered. That is, depending on the Actual Total Daily Dose, multiples of these tablets of strength 100 mg are used for treatment.

The fact that different tablet strengths are used to target a particular Actual Total Daily Dose requires a correction factor (named Factor X) to derive the correct total dose used (see below):

- Factor X = 1: for log lines with an Actual Total Daily Dose of 50 mg or 100 mg.
- Factor X = 2: for log lines with an Actual Total Daily Dose of 20 mg or 200 mg.
- Factor X= 3: for log lines with an Actual Total Daily Dose of 300 mg.
- Factor X=4: for log liens with an Actual Total Daily Dose of 400 mg.

Venetoclax is dispensed weekly during ramp-up, or in 28 days Cycles after ramp-up. Compliance will be calculated on the basis of the *planned* dose and actual total dose *used* per Cycle.

- The total ***planned*** dose for a particular treatment period (e.g., one week treatment with a particular dose during ramp up) can be calculated as follows:

  - **For patients and Cycles with one eCRF log line:**
    Actual Total Daily Dose as entered in the eCRF [mg] x Number of days on treatment.

  - **For patients and Cycles with two or more eCRF log lines (e.g., two log lines in case of one dose change, or treatment interruption with re-initiation in the same Cycle):**
    E.g., for two log lines:
    [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 1) x (Number of days on treatment in log line 1)] + [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 2) x (Number of days on treatment in log line 2)].

    Note: Actual Total Daily Dose may be identical for different log lines (in case of interruption), or different in case of dose change.

- The total dose ***used*** per Cycle can be derived as follows:

  - **For patients and Cycles with one eCRF log line:**
    (Actual Total Daily Dose as entered in the eCRF [mg] / Factor X) x (Number of tablets dispensed – Number of tablets returned).

  - **For patients and Cycles with two or more eCRF log lines:**

    - **All log lines contain information on the number of tablets dispensed, and number of tablets returned (in case of dose change):**
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 1 / Factor X) x (Number of tablets dispensed in log line 1 – Number of tablets returned in log line 1)] +
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 2 / Factor X) x (Number of tablets dispensed in log line 2 – Number of tablets returned in log line 2)].

    - **All log lines for a particular Cycle contain the information on the number of tablets dispensed, and only the last log line for a particular Cycle contains the information on number of tablets returned (in case of treatment interruption and re-initiation of treatment in the same Cycle):**
      [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 1 / Factor X) x (Number of tablets dispensed in log line 1(] - [(Actual Total Daily Dose as entered in the eCRF [mg] in log line 2 / Factor X) x (Number of tablets returned in log line 2)].

- Calculation of compliance for a particular Cycle (%):

  (sum of total dose *used* for all log lines pertaining to a particular Cycle) / (sum of total *planned* dose for all log lines pertaining to a particular Cycle) * 100.

MOR00208

A patient will be considered compliant with the protocol if the MOR00208 dose administered is >80% and ≤120% of the planned dosage per single infusion. Therefore MOR00208 compliance will be presented for each infusion.

Furthermore, MOR00208 dosage will be summarized by cycle as well. The total administered dose per cycle will be divided by the total planned dose per cycle. One MOR00208 dose can be missed between Cycles 1-3, between Cycles 4-12 and one dose between Cycles 13-24 without the patient being non-compliant (skipped doses of MOR00208 due to toxicity will not be considered for calculation of compliance).

A summary displaying the number and percentage of patients in the following categories will also be presented for each study drug, and each cycle:

- ≤80%
- >80 – 120%
- >120%

4.8 Efficacy Analysis

4.8.1 Secondary Endpoint

Single efficacy variable analyzed in this study is: **Best Objective Response Rate (ORR)**

(Best) ORR is defined for Cohort A as percentage of patients achieving a complete response (CR), a partial response (PR) or a partial response with lymphocytosis (PRL) at any time during the study, and for Cohort B as percentage of patients achieving a CR or a PR at any time during the study based on the local assessment. CR, PR or a PRL is defined according to the criteria of the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) for CLL patients (Hallek et al., 2008; see Section 6.3), with the modification that treatment-related lymphocytosis in the absence of other signs or symptoms of disease progression will not be considered as progressive disease (Cheson et al., 2012; Hallek et al., 2012; NCCN NHL 2015 Guidelines). For patients with SLL, assessments will be performed using the Lugano Classification criteria for SLL patients (Cheson et al., 2014). The number of patients and rates will be reported split by cohort.

For derivation of the best ORR, response assessments after a patient has started a new anti-neoplastic therapy will not be taken into account.

Response evaluations (CR, PR, PRL, SD and PD) will be tabulated with counts and percentages for each available visit. Missing response evaluations, or non-evaluable assessments will be taken into account, with patients with missing responses included in the denominator for calculating rates.

The above summary/analysis will be performed using the FAS and PPS.

4.9 Additional Analyses

4.9.1 Immunogenicity Analysis

1. The results of the anti-MOR00208 antibody assessment will be listed for each anti-MOR00208 sample analyzed. The analysis will be performed using the IAS.

Note: For 2. and 3. below, “negative” is defined as a sample reported negative in the screening assay OR confirmatory assay. “Positive” is defined as a sample being reported positive in the confirmatory assay.

Furthermore, the absolute number and percentage of the following categories will be tabulated by visit:

2. Patient has positive anti-MOR00208 antibodies (yes/no/missing):
    - yes, if a titer is available
    - no, if result is reported as negative
    - missing, if anti-MOR00208 measurement is not available

3. In addition, the absolute number and percentage of patients who develop anti-MOR00208 antibodies will be tabulated using the following categories:
    - yes, if the patient has at least one positive post-baseline sample containing anti-MOR00208 antibodies, baseline sample has to be tested negative
    - no, if baseline as well as all post-baseline results are negative
    - not evaluable, if the baseline sample of the respective patient was tested positive
    - missing, if no post-baseline anti-MOR00208 measurement is available

4. Results (n, mean, StD, median, minimum, maximum) of semi-quantitative anti-MOR00208 antibody titer determinations of confirmed positive samples assessments will be tabulated by visit.

4.9.2 Pharmacokinetic Analysis

Individual plasma samples for the analysis of MOR00208 PK will be collected on various study days. For evaluation of PK metrics, patients will be considered who have at least one quantifiable MOR00208 serum concentration (the PK analysis set, PKAS).

Bioanalytical Assessment of Pharmacokinetic Serum Samples

MOR00208 concentration values for each serum sample are to be determined using a validated Ligand Binding Assay. A separate bioanalytical phase plan and report will be generated that provide details on samples handling and processing, methods used for sample analysis, statements on quality control/quality assurance (QC/QA) and results of the each individual sample analyzed for each patient by the bioanalytical labs.

Data Analysis

MOR00208 serum concentrations will be summarized based on nominal (scheduled) sampling times. Serum concentrations below the limit of quantification or missing data will be labelled as such in the concentration data listings. Analyte concentrations that are below the limit of quantification (BLQ) will be assigned a value of zero when they precede the first quantifiable sample. All other BLQ samples will be treated as missing data. Summary statistics for MOR00208 serum concentrations will include n, arithmetic mean, standard deviation, geometric mean, coefficient of variation (CV), median, minimum and maximum. The CV will be expressed as a percentage and calculated as follows:

- CV of the arithmetic mean (%) = standard deviation/mean*100
- CV of the geometric mean (%) = sqrt(exp(variance for log transformed data)–1)*100.

Concentration figures (linear and log y-axis) of mean concentrations ± standard deviation (StD) will be presented. Individual MOR00208 serum concentrations may be excluded from summary statistics and concentration figures (mean) if the actual collection time/date of the sample exceeds allowable windows relative to the scheduled collection time/date.

- For samples collected 1h after the end of MOR00208 infusion, results will be excluded from summary statistics if the deviation of the actual collection time is larger than ± 15 min from the scheduled collection time.
- Results of PK samples collected outside of the allowed window (in days) relative to the scheduled collection day will be excluded from summary statistics. Each 28 day cycle will be considered separately.

Irrespective of exclusion of data points from summary statistics, each obtained MOR00208 serum concentration will be listed and reported.

Accumulation of MOR00208 will be investigated by comparing the average concentration of pre-dose and the average concentration 1 hour post-dose of Cycle 3 Day 1 (i.e. the 10th dose) with the

corresponding mean from the previous visit for which MOR00208 concentration data is available using analysis of variance (ANOVA) ($\alpha = 0.05$). If no significant difference is found, Cycle 3 Day 1 will be compared to previous visit for which MOR00208 concentration data is available and so forth until two consecutive times a significant difference is found.

Furthermore, additional PK sample assessment may be performed to determine bioactive MOR00208 serum concentrations. These MOR00208 serum concentrations will only be reported in listings and none of the above described PK analyses (tables, figures) will be performed using these bioactive MOR00208 serum concentrations.

4.9.3 Assessment of MRD Response

Patients who develop a PR or CR will be assessed using MRD testing from peripherial blood (PB) at C1D1, C4D1, C7D1, C13D1, etc. until bone marrow (BM) MRD negativity was confirmed. An additional PB sample will be obtained from CR patients at the time when CR is confirmed by CT outside of the scheduled radiological examinations. Additionally, patients with CR or PR will be further assessed for MRD negativity status from bone marrow (aspirate) at least 8 weeks after the PB MRD negativity was detected (for patients with CR only after CR has been confirmed by CT/MRI scan).
The results of MRD testing for CR and PR patients (MRD positivity/MRD negativity assessed in PB; MRD positivity/MRD negativity assessed in BM) will be tabulated with counts and percentages for each available visit and overall. The median time to MRD negativity assessed in PB and BM will be calculated for CR and PR patients (including only patients who reached MRD negativity).

4.9.4 Biomarkers

Blood and protein biomarkers which are important in the mechanism of action of, or could predict response to, the study drugs will be descriptively tabulated, presenting absolute and change to baseline values, if applicable. A separate validation plan and standard operating procedures (SOPs) for the flow cytometry based biomarkers will be generated that provide details on samples handling, processing and methods used for sample analysis.

Biomarker assessments will be tabulated by descriptive statistics. Summaries for baseline values will be provided for the following variables:

- CD16 molecules on $CD16^{+}CD56^{+}$ NK cells (continuous variable)
- FcγRIIIa affinity (categorical variable):
    - 2 subgroups (high affinity: FCGR3A-158V homozygosity vs. low affinity: FCGR3A-158F homozygosity, or FCGR3A-158F/V heterozygosity)
    - 3 subgroups (FCGR3A-158V homozygosity vs. FCGR3A-158F homozygosity vs. FCGR3A-158F/V heterozygosity)
- FcγRIIa affinity (categorical variable):
    - 2 subgroups (high affinity: FCGR2A-131H homozygosity vs. low affinity: FCGR2A-131R homozygosity, or FCGR2A-131H/R heterozygosity)
    - 3 subgroups (FCGR2A-131H homozygosity vs. FCGR2A-131R homozygosity vs. FCGR2A-131H/R heterozygosity)
- NK cell numbers/µl at baseline (continuous variable)
- Longitudinal analyses:

  Longitudinal analyses will be conducted separately for:
    - Peripheral numbers of NK cells
    - B cells (defined as the sum of the following cell populations: “Abs_B cell_CD5+ [T3]” and “Abs_B cell_CD5neg [T3]”)
    - T cells

- CD19 molecules on CD5-positive B cells (defined as "CD19mol/CD5+CD19+Bcells_BL" or "CD19mol/CD5+22neg19+_BL" at Cycle 1 Day 1, and as "CD19mol/CD5+22neg19+_AW" at following visits)
- CD19 molecules on CD5-negative B cells (defined as "CD19mol/CD5neg22neg19+_BL" at Cycle 1 Day 1, and as "CD19mol/CD5neg22neg19+_AW" at following visits)

The following summaries and graphs will be produced:

- Summary statistics per visit (a 95% confidence interval for the median will be derived by bootstrapping)
- Summary for the relative change from baseline (a 95% confidence interval for the median will be derived by bootstrapping).
- Graphical illustration showing individual values for both absolute values and separately relative change from baseline. The median across all patients by treatment (without confidence interval) will be shown.
- Graphical illustration showing the median and its 95% confidence interval (via bootstrapping) for both absolute values and relative change per visit across all patients assessed by treatment.
- Graphical illustration showing boxplots for both absolute values and relative change per visit across all patients assessed by treatment.

All biomarker analyses will be conducted on the FAS.

4.10 Safety Analysis

The analysis of safety assessment in this trial will include summaries of the following categories of safety and tolerability data collected for each patient:

- Adverse Events (number and severity)
  - Treatment-emergent adverse events (TEAEs)
  - Treatment-emergent serious adverse events (SAEs)
  - TEAEs by maximum toxicity grade
  - TEAEs by intensity
  - Drug related TEAEs
  - TEAEs leading to discontinuation of treatment
  - TEAEs leading to any action on study medication (i.e., interruption, dose reduction, permanent discontinuation)
  - Treatment-emergent AESI
  - TEAEs leading to death
- Vital signs: systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate, pulse rate and temperature
- Physical Examination
- 12-lead ECG parameters: PR, QRS, RR and QT interval values
- Laboratory safety evaluations (blood chemistry, hematology, coagulation, urinalysis)
- ECOG Performance Status

- B-symptoms

All safety variables will be summarized using the SAF split by actual treatment.

4.10.1 Adverse Events

An AE is defined as any untoward medical occurrence in a patient or participant in a clinical trial administered a medicinal product, which does not necessarily have a causal relationship to this treatment.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to that study drug. AEs include any clinically significant deterioration of a patient's medical status after the signing of the informed consent form (ICF). Also, an increase in the frequency or intensity of a pre-existing event or conditions and events resulting from protocol mandated procedures (e.g., invasive procedures) fall under the definition of AEs.

In addition, overdoses exceeding the planned infusion dose by 20% should be recorded as AEs.

Please note that in the context of this protocol symptoms that are clearly associated to the progression of underlying malignancy (CLL/SLL) do not fall under the definition of AEs.
Each AE will be reported to determine the following:

- Relationship to the study drug(s) (suspected/not-suspected)
- Duration (start and end date, or if continuing at end of study)
- NCI-CTCAE Grade (see 4.10.1.5)
- Intensity: the intensity of all AEs will be graded as mild, moderate, or severe using the following definitions:
    - mild: tolerable
    - moderate: interferes with normal activity
    - severe: incapacitating (causes inability to perform usual activities or work)
- Outcome (i.e., Not Recovered/Not Resolved, Recovered/Resolved, Recovered/Resolved with sequelae, Recovering/Resolving, Fatal, Unknown)
- Action taken with study drug(s)
    - no action taken
    - study drug temporarily interrupted
    - study drug permanently discontinued due to this AE
- Other action taken (medication taken; non-drug therapy given; hospitalisation/ prolonged hospitalisation)
- Seriousness: whether it is serious, where an SAE is defined as one that:
    - results in death
    - is life-threatening
    - requires inpatient hospitalisation or prolongation of existing hospitalisation (hospitalisation signifies that the patient was an inpatient for at least one overnight stay) unless hospitalisation is for:
        - Routine treatment or monitoring of the studied indication, not associated with deterioration of symptoms related to CLL/SLL
        - Elective or pre-planned treatment for a pre-existing condition that is unrelated to CLL/SLL and has not worsened since signing of the ICF

- Social reason and respite care in the absence of any deterioration in the patient's general condition

- Results in persistent or significant disability or incapacity
- Is a congenital anomaly or birth defect
- Is medically significant, i.e., defined as an event that jeopardizes the patient or may require medical intervention to prevent one of the outcomes listed previously

4.10.1.1 Treatment-emergent adverse events (TEAEs)

An **on-treatment adverse event (or Treatment-emergent Adverse Event – TEAE)** is defined as:

- An adverse event that occurred in the following time interval (including the lower and upper limits):
  - date of first administration of study treatment
  - until 30 days after last study drug administration
- An adverse event present prior to the study treatment start but increased in severity after treatment start.
- An adverse event occurring or worsening later than 30 days after the last treatment if suspected to be related to the study drug.

If the last date of study drug administration is missing, on-treatment assessments/events include any assessment/event recorded in the database and which occur after the start date of study treatment. Safety summary tables including summaries of on-treatment deaths will be based only on on-treatment assessments/events.

An AE present prior to the study treatment start but increased in severity after treatment start, will also be included as TEAE.

The handling of partially of completely missing AE start and end dates/times in the determination of the status of the AE is described in detail in Section 4.14.1.

The incidence of treatment-emergent AEs will be summarized in incidence tables. If a patient experiences more than one occurrence of the same AE, the occurrence with the highest toxicity grade/greatest severity and the closest association with the study drug will be counted in the summary tables. All AEs will be listed by patient, along with information regarding onset, duration, relationship to study drug, intensity, toxicity grade, action taken with study drug, treatment of event, and outcomes.

4.10.1.2 Adverse events of special interest

AEs of special interest (AESIs) for MOR00208 are: tumor lysis syndrome (TLS), infusion-related reactions (IRRs) and allergic reactions to study drug ≥ grade 3, cytokine release syndrome and overdoses of MOR00208.

AEs of special interest (AESIs) for idelalisib are: Diarrhea/colitis ≥ grade 3, pneumonitis ≥ grade 3 and elevation of hepatic enzymes ≥ grade 3, Pneumocystis jirovecii pneumonia (PJP), Cytomegalovirus (CMV) infections, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) and overdoses.

AEs of special interest (AESIs) for venetoclax are: TLS, neutropenia with infection or fever ≥ grade 3 and overdoses.

Unlike routine safety assessments, SAEs and AESIs are monitored continuously and have special reporting requirements.

4.10.1.3 Relationship to study drug

The Investigator should determine the causality (relationship to the study drug) based on his/her clinical experience and on the information given in the Investigator's Brochure (IB) for MOR00208 and the SmPC/prescribing information for idelalisib/venetoclax. The causal relationship of all AEs to the study drug will be judged as either suspected or not suspected. A suspected causal relationship means at least a reasonable possibility that the event is caused by the study drug. If no relationship has been provided by the Investigator, the event will be considered as related to the study drug.

4.10.1.4 Coding of adverse events

Adverse events will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA) and will be reported by primary system organ class (SOC) and preferred term (PT). The MedDRA version used for reporting the study will be the version used for coding the trial and will be specified in the clinical study report and as a footnote in the related outputs (if possible).

4.10.1.5 Grading of adverse events

Toxicity grade: determined according to the National Cancer Institute- Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 of June 14, 2010 (or higher), using the following definitions:

- Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- Grade 2: moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.)
- Grade 3: severe or medically significant but not immediately life-threatening; hospitalisation or prolongation of hospitalisation indicated; disabling; limiting self-care activities of daily living
- Grade 4: life-threatening consequences; urgent intervention indicated
- Grade 5: death related to AE

The CTCAE represents a comprehensive grading system for reporting the acute and late effects of cancer treatments. CTCAE grading is by definition a 5-point scale generally corresponding to mild, moderate, severe, life threatening, and death. This grading system inherently places a value on the importance of an event although there is not necessarily proportionality among grades (a grade 2 is not twice as bad as a grade 1).

4.10.1.6 General rules for reporting

4.10.1.6.1 AE tables

i. All safety analyses will be done using the Safety Set and will be presented by cohort, and overall across both cohorts
ii. The incidence of treatment-emergent AEs will be summarised in incidence tables.
iii. AEs will be summarised by SOC and PT using the Medical Dictionary for Regulatory Activities (MedDRA) version 19.0 and will be updated to the most current version at the end of the trial. The SOCs and PTs will be used for tabulation.
iv. AE frequency tables will display the number of events (incidence), number of patients experiencing an event and the percentage of patients with the event by System Organ Class (SOC) and Preferred Term (PT).

v. If a patient experiences more than one occurrence of the same AE, the occurrence with the greatest severity and the closest association with the study drug will be counted in the summary tables.
vi. If a patient reported more than one AE with the same preferred term, the AE with the maximum toxicity grade will be presented.
vii. If a patient reported more than one AE within the same primary system organ class, the patient will be counted only once with the maximum toxicity grade at the system organ class level, where applicable.
viii. The most common AEs reported (≥10 % for each preferred term) will be presented in descending frequency according to its incidence starting from the most common event.
ix. All safety variables will be summarized using the SAF split by actual treatment.

4.10.1.6.2 AE listings

i. In the AE listings, AEs that started prior to the administration of any study drug will be flagged as pre-treatment AEs. AEs that start 30 days after the last study treatment and which are not related to one of the study drugs will be flagged as post-treatment AEs.

ii. Special AE listings displaying details of the event(s) captured on the eCRF in a compact format will be provided for:

- Treatment-emergent Serious Adverse Events.
- TEAEs suspected to be related to study drug
- Treatment-emergent SAEs suspected to be related to study drug
- TEAEs of toxicity grade 3 or grade 4.
- TEAEs leading to interruption of treatment (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).
- TEAEs leading to discontinuation of treatment (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).
- TEAEs of special interest.
- AEs leading to death (i.e., AEs of grade 5).
- Pre-treatment AEs (for subjects that were successfully screened but not treated).

iii. All AEs will be listed by patient, along with information regarding onset, end date (if not ongoing), relationship to study drugs, intensity, toxicity grade, action taken with study drug, and outcomes. This listing will be generated for all patients enrolled.

4.10.1.7 AE summaries

4.10.1.7.1 TEAEs (serious and non-serious)

The following summaries will be provided:

i. All TEAEs regardless of study treatment relationship by primary SOC, PT and grade.

ii. All TEAEs regardless of study treatment relationship by primary SOC, PT and intensity.

iii. Most frequent TEAEs *(at least in 10% of the patients)* regardless of study treatment relationship by SOC, PT and grade.

iv. TEAEs regardless of study treatment relationship ≥ grade 3 by primary SOC, PT and grade.

v. TEAEs regardless of study treatment relationship of grade 3 or grade 4 by primary SOC, PT and grade.

vi. TEAEs regardless of study treatment relationship starting in Cycle 1 (reported for Cohort A only).

vii. TEAEs regardless of study treatment relationship starting before Cycle 2 Day 15 (reported for Cohort B only).

viii. TEAEs suspected to be related to the study drug by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).

ix. TEAEs suspected to be related to the study drug by primary SOC, PT, and intensity (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).

x. TEAEs suspected to be related to the study drug of ≥ grade 3 by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).

xi. TEAEs suspected to be related to the study drug of grade 3 or grade 4 by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 and idelalisib/venetoclax, or any study drug).

xii. Most frequent TEAEs suspected to be related to the study drug *(at least in 10% of the patients)* by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 and idelalisib/venetoclax, or any study drug).

xiii. TEAEs leading to any action on MOR00208, on idelalisib/venetoclax, on both MOR00208 and idelalisib/venetoclax, or any study drug regardless of study treatment relationship by primary SOC, PT and grade.
Note: Any Action = Dose reduction/Dose interruption/Permanent discontinuation.

xiv. TEAEs leading to discontinuation of treatment (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug) regardless of study treatment relationship by primary SOC, PT and grade.

xv. TEAEs leading to interruption of treatment (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug) regardless of study treatment relationship by primary SOC, PT, and grade.

xvi. Most frequent non-serious TEAEs, regardless of study treatment relationship by primary SOC, PT and grade (at least 5% incidence).

4.10.1.7.2 Treatment-emergent SAEs

The following summaries on treatment-emergent SAEs will be provided:

- Treatment-emergent SAEs regardless of study treatment relationship, by primary SOC, PT and grade.
- Most frequent treatment-emergent SAEs *(at least in 2% of the patients)* regardless of study treatment relationship, PT and grade.
- Treatment-emergent SAEs starting in Cycle 1 for Cohort A.
- Treatment-emergent SAEs starting before Cycle 2 Day 15 for Cohort B.
- Treatment-emergent SAEs regardless of study treatment relationship ≥ grade 3 by primary SOC, PT and grade.
- Treatment-emergent SAEs of grade 3 or grade 4 regardless of study treatment relationship by primary SOC, PT and grade.
- Treatment-emergent SAEs suspected to be related to the study drug by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).

- Treatment-emergent SAEs suspected to be related to the study drug ≥ grade 3 by primary SOC, PT, and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).
- Treatment-emergent SAEs suspected to be related to the study drug of grade 3 or grade 4 by primary SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).
- Most frequent Treatment-emergent SAEs suspected to be related to the study drug *(at least in 2% of the patients)* by SOC, PT and grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, and any study drug).
- Treatment-emergent SAEs of grade 5 by primary SOC and PT.

4.10.1.7.3 AESIs

Treatment-emergent AEs of special interest will be presented by primary SOC, PT and grade.

4.10.1.7.4 Deaths

All deaths will be summarized as follows:

- Deaths related to disease progression as indicated on the '*End of Treatment*' eCRF page:
  - Any entry containing the phrase "PROGRESSIVE DISEASE" or "DISEASE PROGRESSION" or "LYMPHOMA PROGRESS" in the log line '*Primary Reason: Death, please specify cause of death*' will indicate PD-related deaths.
- Deaths unrelated to disease progression as indicated on the '*End of Treatment'* eCRF page:
  - All other deaths that are not considered as related to disease progression.

4.10.1.7.5 Overall AE summary table

In addition, an **Overall AE summary table** will be presented showing the incidence and number of patients with at least one of the events:

- At least one TEAE regardless of study treatment relationship.
- At least one treatment-emergent SAE regardless of study treatment relationship.
- Deaths (split by related to disease progression vs. unrelated to disease progression).
- At least one treatment-emergent SAE suspected to be related (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).
- At least one TEAEs suspected to be related to the study drug by grade (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).
- At least one TEAE suspected to be related to the study drug with grade 3 or grade 4 (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).
- At least one TEAE suspected to be related by intensity (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).
- At least one treatment-emergent AESI.
- At least one TEAE leading to any action on MOR00208, on idelalisib/venetoclax, on both MOR00208 *and* idelalisib/venetoclax, or on *any* study drug).

  Note: Any Action = Dose reduction/Dose interruption/Permanent discontinuation.
- TEAEs leading to discontinuation of treatment (split by MOR00208, idelalisib/venetoclax, both MOR00208 *and* idelalisib/venetoclax, or any study drug).

- SAEs of grade 5.
- At least one TEAE of PT 'infusion-related reaction (IRRs)' of ≥ grade 3 by grade.

4.10.2 Vital Signs

Systolic and diastolic blood pressure (mmHg), heart rate (beats per min), respiratory rate (breaths per min) and temperature assessed will be descriptively summarized using the SAF. The vital signs data will be listed by patient and date of assessment. Each abnormal value will be flagged to show whether it is a value below or above the normal limit. Normal ranges for vital signs will be defined as follows:

Systolic blood pressure: 70-149 mm Hg

Diastolic blood pressure: 60-90 mm Hg

Heart rate: 55-110 beats per minute

Respiratory rate: 10-24 breaths per minute

Body temperature: 36.1-37.8 °C

4.10.3 Physical Examination

A complete physical examination (PE) will be performed at screening and at the end of the treatment period.

Limited PEs may be focused on tumor response assessment (lymph nodes, liver, spleen, etc.) and AEs (e.g. attention on respiratory signs and symptoms) at the Investigator's discretion. Such limited PEs will be performed as indicated in the Schedule of Assessments (Table 1). Limited PE will be performed on Day 1 and 15 of Cycle 1 to 6, and on Day 1 of all further cycles. Symptom-driven full PEs may be performed as clinically indicated at any study visit.

The number and percentage of patients experiencing an abnormal physical examination finding will be presented per body system using the SAF. Physical examination assessments will be listed per body system by patient and date of assessment.

4.10.4 12-lead ECG

Summary ECG assessments (normal; abnormal clinically significant; abnormal not clinically significant) will be tabulated by time point (visit) using frequencies.

ECGs will be shown in a listing and overall interpretations will be flagged to show whether the ECG is considered normal; abnormal clinically significant; abnormal not clinically significant. Each abnormal PR, QRS, RR and QT interval value will be flagged to show whether it is a value below or above the normal limit. The following normal ranges will be applied:

PR interval: 110-220 ms

QRS interval: 60-120 ms

RR interval: 600-1200 ms

QT interval: ≤ 400 ms

Descriptive summaries of actual values and changes from baseline will be presented by visit for ECG measures of RR interval, PR interval, QRS interval, and QT interval. The number of patients having a QT interval > 500 ms will be summarized by visit.

4.10.5 Laboratory Findings

Descriptive statistics for Clinical laboratory data will be summarized. Actual values and the change from baseline will also be summarized along with the numbers of patients with values outside limits of the normal range at each timepoint. The laboratory analysis tables will be presented using the SAF.

Shift tables of baseline to the worst post baseline toxicity grade in chemistry and hematology tests will be provided. For a given patient, if the toxicity grade is missing for all post baseline assessments for one laboratory test, the patient will be counted only once for that laboratory test under the "Missing" toxicity grade category.

Laboratory toxicities will be graded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 4.03 or higher.

If a patient has both missing and non-missing toxicity grades for one laboratory test, the missing toxicity grade of that laboratory test will be treated as the lowest grade. For each test condition, percentages are calculated based on the number of patients in the SAF population who have a baseline and at least one post-baseline assessment.

Laboratory tables and listings will be based on the safety analysis set. Pregnancy test results will be only listed.

The laboratory parameters displayed in **Table** recorded at Screening and during the treatment and additional treatment period will be used for listing and table summary.

Abnormal values will be flagged to indicate whether the value is below or above the reference range and whether investigators assessed the abnormal value as clinically significant. A clinically significant result can be commented with "Adverse Event", "Due to primary disease", "Pre-existing condition and not worsened according to CTCAE 4.03" or free text.

Table 4: Safety Laboratory Evaluations

Evaluation	Analysis
"Emergency laboratory" (EDTA blood and serum sample)	AST, ALT, bilirubin (total, direct and indirect), direct Coombs test, hemoglobin, platelets, potassium, serum creatinine, sodium, WBCs, including WBC differential (including ANC) [1] Cohort B only: Additional values to be analyzed: calcium, creatinine, inorganic phosphorus (phosphate), potassium and uric acid
Hematology (EDTA blood)	Direct Coombs test, erythrocyte count (RBC count), hematocrit, hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, platelet count, reticulocytes, WBC with differential count (absolute counts and % of leukocytes: basophils, eosinophils, lymphocytes, monocytes, neutrophils) At screening: should include a peripheral blood smear.
Serum chemistry (serum sample)	ALT, total albumin, ALP, amylase, AST, β_2-microglobulin, bicarbonate, bilirubin (total, direct and indirect), blood urea nitrogen, calcium (total), chloride, cholesterol, creatinine, creatinine kinase, GGT, glucose, LDH, lipase, magnesium, phosphate, potassium, protein (total), serum CrCl calculated using a standard Cockcroft-Gault formula[2], sodium, triglycerides, uric acid
Coagulation parameters (sodium citrate blood)	Activated partial thromboplastin time, prothrombin time, international normalized ratio

Viral parameters (serum or plasma sample)	Hepatitis B: HBsAg, anti-HBc and HBsAb. HBV DNA if anti-HBc positive, optional Hepatitis C: HCV antibody (HCV RNA quantification if anti-HCV positive) CMV: CMV antibody and CMV copy number per mL (PCR based) HIV-1/-2 Ag and Ab Screening (HIV-1/-2 Ab differentiation if HIV positive)
Pregnancy test (serum sample)	β-HCG serum, females of childbearing potential only
Pregnancy test (urine)	β-HCG urine, females of childbearing potential only
Urinalysis	Clarity (clear, slightly cloudy, cloudy, turbid), bilirubin, color, glucose, hemoglobin, ketones, leukocyte esterase, nitrite, pH, protein, specific gravity, urobilinogen. Microscopy will only be performed if clinically indicated.

Abbreviations: ALP= alkaline phosphatase; ALT=alanine transaminase; anti-HBc=hepatitis B core antibody; ANC=absolute neutrophil count; AST=aspartate amino-transferase; β-HCG=beta-human chorionic gonadotropin; CMV=Cytomegalovirus; CrCl=creatinine clearance; DNA=deoxyribonucleic acid; EDTA=ethylenediaminetetraacetic acid; GGT=gamma-glutamyltransferase; HBsAb=hepatitis B surface antibody; HBsAg=hepatitis B surface antigen; HBV=hepatitis B virus; HIV=human immunodeficiency virus; LDH=lactate dehydrogenase; PCR=polymerase chain reaction; RNA= ribonucleic acid; RBC=red blood cell; WBC=white blood cells.
[1]WBC differential can be automated or manual as per institutional standards. Reticulocytes may be determined only when clinically indicated.
[2]For the Cockcroft-Gault formula, see Appendix B.

4.10.6 ECOG Scores Analyses

The analysis of ECOG scores will be performed on the SAF.
The following analyses will be performed on ECOG scores:

- The ECOG performance status will be summarized categorically in a frequency table by visit.
- Shift Tables in ECOG status from baseline to worst post-baseline will be presented.

Listings showing ECOG scores will be generated.

4.10.7 B-Symptoms

B-symptoms are defined as any one or more of the following disease-related symptoms or signs:

- Unintentional weight loss of ≥ 10% within the preceding 6 months or less.
- Drenching night sweats without signs of infection.
- Recurrent, unexplained fever with temperatures above 38°C without signs of infection.

The presence of B-symptoms will be summarized categorically in a frequency table by visit. The analysis will be performed on the SAF. Data listings will be presented.

4.11 Other Data

All other data collected in the eCRF will be listed.

4.12 Protocol Deviations

Key protocol deviations will be summarized overall and by center and grouped into the following categories prior to database lock:

- Prohibited concomitant medication

- Informed consent form
- Eligibility criteria
- Laboratory assessment
- Procedure or test
- Study drug and treatment
- Visit schedule and assessment

Other Only protocol deviations directly affecting the patient will be reported. Protocol deviations pertaining to the study centers will not be considered.

The number (%) of patients in the SAF with at least one of the above protocol deviations will be tabulated.

Protocol deviations leading to exclusion from the PPS will be identified before database lock. Those protocol deviations leading to exclusion from the PPS will be tabulated and listed for the FAS. All key protocol deviations will be listed.

4.13 Independent Data Monitoring Committee

An IDMC will be established by the sponsor to review the safety run-in phase and accumulating safety data at regular intervals throughout the study and monitor overall study conduct. The IDMC will also evaluate results of a futility analysis described in Section 12.10 of the Clinical Study Protocol. The IDMC will be composed of experts in the field of oncology and clinical biostatistics who have no other role in the study and do not have an affiliation with the Investigators or the sponsor. Based on the safety and efficacy data, the IDMC recommends in writing to the sponsor whether or not to stop the clinical study or a specific cohort. The IDMC's specific duties as well as statistical monitoring guidelines and procedures will be fully described in an IDMC Charter.

4.14 Handling of Missing Data and Outliers

4.14.1 Missing Data

The number of patients with missing data will be presented under a "Missing" category. Missing values will be included in the denominator count when computing percentages.

When continuous data are being summarized, only the non-missing values will be evaluated for computing summary statistics.

Efficacy analyses:

In the responder analysis (ORR), patients with missing data will be considered as non-responders.

Analyses on previous and concomitant medications:

In case of missing or incomplete dates not directly allowing allocation to any of the categories of medications, a worst-case allocation will be done according to the available parts of the start and the end dates for:

- Concomitant medication
- Medication maintained during the treatment period
- Post-study medication
- Previous medication

Safety analyses:

In case of missing or incomplete dates not directly allowing allocation to any of the categories of AEs, a worst-case allocation will be done according to the available parts of the start and the stop dates. The AE will be allocated to the first category allowed by the available data, according to the following order:

- Treatment-emergent
- Post-study
- Pre-treatment

Other critical missing data, if any, will be discussed during the review of the data. Decisions will be fully documented.

The following approach will be taken to impute only partially completed dates

- Only for AESI: If the start time of an AESI is missing but the start date is complete, this AESI will only be excluded from treatment-emergent AEs if start day is before day of first treatment or start day is after end day of treatment-emergent period.
- If the start day is missing but the start month is complete, an AE will only be excluded from treatment-emergent AEs if start month is before month of first treatment or start month is after end month of treatment-emergent period or if stop date (and time in case of an AESI) is before start of first treatment.
- If start day and month are missing but the start year is complete, an AE will only be excluded from treatment-emergent AEs if start year is before year of first treatment or if start year is after end year of treatment-emergent period or if stop date (and time in case of an AESI) is before start of first treatment.

If start date is completely missing, an AE will not be excluded from treatment-emergent AEs unless the stop date (and time in case of an AESI) is before start of first treatment.

Time since first CLL/SLL diagnosis:

The time since first CLL/SLL diagnosis (reported in months), i.e., the interval between date of first diagnosis and Screening Visit, will be summarized.If the date of diagnosis is incomplete, the time since first diagnosis will be calculated based on the latest possible date for the date of diagnosis:

- If the day is missing but the month is complete for date of diagnosis, the date will be amended using day 15 of that month (or the date of screening visit in case this is earlier)
- If the day and month are missing but the year is complete for date of diagnosis, the date will be amended using June 30 of that year (or the date of screening visit in case this is earlier)

Duration of response to last previous therapy line:

Duration of response for the last previous therapy is defined as the elapsed time between the date of first documented response (CR or PR) under this therapy and the date of documented progression after that.

- If day is missing for the date of initial response or the date of progression and month and year are present, the following worst case imputation will be done: the last day of the respective month will be used to amend the date of initial response and the first day of the respective month will be used to amend the date of progression. In case this approach leads to contradictive dates which can only happen if month and year are the same for both dates either the missing date the duration of response will be set to 1 day.
- If day and month for the date of initial response or the date of progression are missing the following worst case imputation will be done if it does not lead to contradictive dates: for initial response December 31st of the pertaining year will be used and for date of progression January 1st of the pertaining year. If a date of best overall response is present and it is before the imputed date of initial response this date will be used as a substitute. If the imputed days remain contradictive the duration of response will be set to 1 day. If year is missing for the

date of progression no imputation will be done and the duration of response will be treated as missing. If year is missing for date of initial response but a date of best overall response is (at least partially) present this date will be used for the calculation of duration of response. If both dates of initial and best overall response are missing no imputation will be done.

Time since completion of last prior therapy:

The following algorithm will be used to impute partially completed dates required to calculate the time since completion of the last prior therapy:

- If day and month are missing but year is available, then the imputed day and month will be January 1st or the starting date of the last regimen, whichever is later;
- If day is missing but the month and year are available, then the imputed day will be the first day of the month, or the starting date of the last regimen, whichever is later;
- If year is missing, no imputation will be done and the completion date will be treated as missing.

4.14.2 Outliers

No data will be excluded from the analyses, including any outliers.

4.15 Data Handling for Laboratory Data

Laboratory data that are continuous in nature but are less than the lower limit of quantitation or above the upper limit of quantitation will be imputed. The limit of quantitation will be used for calculation of descriptive statistics if the data is reported in the form of "≤ x" or "< x" or "≥ x" (x is considered as the limit of quantitation).

4.16 Deviations from SAP

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

4.17 Changes in Conduct or Planned Analyses from the Protocol

In the SAP a more detailed information was provided for both the definition of the FAS and the SAF. As per SAP the definition for the SAF was extended in a sense that the SAF is based on the treatment actually received. This extension of the definition is justified as the SAF will be used for all safety-relevant analyses, which have to be interpreted in the context of the treatment that has been actually received. Moreover, for the SAF as per SAP the restriction that at least one post-baseline safety evaluation is required was added.

4.18 Output Format

All output will be produced using SAS version 9.4 or a higher version.

In 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 following header will be used for all tables, listings and figures outlined in this document: MOR208C205 – reporting event (Cut-off date ddMONyyyy).

The following labels of reporting event will be used for all outputs:

- PA for Primary Analysis
- FA for Final Analysis

The *SAS program name, source data, page number*, *date and time of creation* of table/listing and the source listing number will be displayed on each table/listing.

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

Tables and listings will be produced in rich text (RTF) format (i.e. they will tabular in format).

The *left* and *right margins* of all tables and listings will be a minimum of 2.0 cm from the left and 2.0 cm from the right. The *top and bottom margins* will be a minimum 2.0 cm. *Header and footer* will both be 1.27 cm.

A *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 patient's record has been continued to the next page, an appropriate identification (e.g., the patient ID number) must be presented at the beginning of that page.

4.19 Software

- SAS® Software Version 9.4 or a higher version. Institute Inc., Cary, NC, USA

4.20 Quality Control of Outputs

The following steps will be taking to ensure the quality of the outputs:

- The author of each table/listing/figure program will review the programs and will verify that no error message is highlighted in the 'LOG' file.
- Type A or Type B validation will be carried out for validating the TLGO and the datasets. Where Type A validation includes, but is not limited to:
  - Independently writing code to produce a validation output.
  - Using an electronic means of comparison (for example, SAS Proc Compare or UNIX diff command) to compare the data and/or output produced by the production programmer to the data and/or output produced by the Independent Validator.
  - Visually inspecting the output to ensure that the layout, format and other cosmetic factors match the requirements and specifications and that the data appear logical and correct.
- Type B validation includes, but is not limited to:
  - Review of the code written by the Production Programmer to ensure that the correct variables and data were used and all data manipulation was conducted using sound programming logic that results in accurate output.
  - Visual inspection of the output is required to ensure that the layout, format and other cosmetic factors match the requirements and specifications and that the data appear logical and correct.

Related outputs will be compared for consistency. The type of validation used for each Analysis Datasets (ADS) and/or TLGO is specified in the Programming Development and Validation Document (PDVD).

4.21 Conventions

Wherever possible, data will be decimal aligned.

Numeric variables will be listed with the same number of decimal places as in the actual data.

The following rules on decimal places will be considered for the results of the analyses (if the analyses are performed on derived variables, the level of precision of the actual data is derived from the previous list):

- Minimum, maximum: same as actual data
- Mean and its confidence limits (unadjusted and adjusted), adjusted difference between means and its confidence limits, median, first and third quartiles: actual data + 1 decimal place, standard deviation (StD): actual data + 2 decimal places. For the tabulation of biomarker there will be an exception if the measurements represent counts. In this case mean, median and quartiles will be displayed without decimal places.
- Percentage: 1 decimal place
- Kaplan-Meier percentiles estimates and confidence limits: actual data + 1 decimal place (3 decimal places for survival probabilities)
- Odds ratio/hazard ratio and its confidence limits: 3 decimal places

Unless otherwise specified frequency tabulations will be presented by number and percentage, where the percentage is presented in brackets.

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.

Unless otherwise stated, listings will be presented by study treatment, and sorted by patient ID. Patient ID will be presented on all listings.

In general, dates will be presented on listings in the format ddmmmyyyy (date9.) and time in the format hh:mm (time5.). In case of partial dates or times, missing information will be replaced by dashes.

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 treatment, patient and visit (unless otherwise specified) and have the study data tabulation model (SDTM) and/or analysis dataset model (ADaM) source data referenced in a footnote.

In stratified tables, each stratum will start on a new page.

5 References

American Statistical Association (ASA). Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, August 7, 1999.

Cheson BD, Byrd JC, Rai KR, Kay NE, O'Brien SM, Flinn IW, et al. Novel targeted agents and the need to refine clinical endpoints in chronic lymphocytic leukemia. J Clin Oncol. 2012;30(23):2820-2.

Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol. 2014;32(27):3059-68.

Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute –Working Group 1996 guidelines. Blood. 2008;111(12):5446-56.

Hallek M, Cheson BD, Catovsky D, et al. Response assessment in chronic lymphocytic leukemia treated with novel agents causing an increase of peripheral blood lymphocytes [letter]. Blood. 2012;119(23):5348.

Hillmen P, Diels J, Healy N, Iraqi W, Aschan J, Wildgust M. Real-World Experience of Ibrutinib in >2900 Chronic Lymphocytic Leukemia Patients: Data from a Global Named Patient Program. Poster #208 EHA 2016.

International Conference on Harmonization; Guidance on Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration [Docket No. 97D-0174]. Federal Register Volume 63, Number 179, pages 49583-49598. September 16, 1998.

Mato AR, Nabhan C, Barr PM, Ujjani CS, Hill BT, Lamanna N, et al., Favorable Outcomes in CLL Patients with Alternate Kinase Inhibitors Following Ibrutinib or Idelalisib Discontinuation. Oral Presentation Abstract 719 ASH 2015

National Comprehensive Cancer Network (NCCN) Guidelines for Treatment of Cancer by Site. Non-Hodgkin's Lymphomas; 2015. https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf.

Note for Guidance on Statistical Principles for Clinical Trials (ICH Topic E9, Step 4) adopted by CPMP, March 1998; issued as CPMP/ICH/363/96.

The Royal Statistical Society (RSA). Code of Conduct; 2014 (revision).

eA phase 1 trial of the Fc-engineered CD19 antibody XmAb5574 (MOR00208) demonstrates safety and preliminary efficacy in relapsed CLL. Blood. 2014a;124(24):3553-60.

6 Appendices

6.1 Appendix A: Binet and Rai Staging System

Binet Staging Stage	Clinical features
A	Lymphocytosis, does not meet criteria for stages B or C
B	≥ 3 areas of lymphadenopathy*, does not meet criteria for stage C
C	Anemia (Hb < 10 g/dL) or thrombocytopenia (platelets < 100 x10^9/L)

* The four lymphadenopathy areas are: cervical, axillary, inguinal, spleen/liver
Adapted from: Binet JL, Auquier A, Dighiero G, Chastang C, Piguet H, Goasguen J, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer. 1981;48(1):198-206.

Modified Rai Clinical Stage Risk category	Clinical features
Low	Lymphocytes > 15 x 10^9/L
Intermediate	As 0 + lymphadenopathy or hepato- or splenomegaly
High	Anemia (Hb ≤ 11 g/dL) or thrombocytopenia (platelets ≤ 100 x10^9/L)

Adapted from: Rai KR. A critical analysis of staging in CLL. In: Gale RP, Rai KR, eds. Chronic Lymphocytic Leukemia: Recent Progress and Future Directions. New York: Alan R. Liss; 1987: 253-64.

The Binet clinical staging system and the modified Rai clinical staging system for CLL comprise three stages.
The use of clinical staging systems is recommended in current CLL guidelines, and can guide the initiation of treatment.

6.2 Appendix B: Cockcroft-Gault Formula

Cockcroft-Gault Equation:

$$eC_{Cr} = \frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times [0.85\ if\ Female]}{72 \times \text{Serum Creatinine (in mg/dL)}}$$

This formula presumes weight to be measured in kilograms and creatinine to be measured in mg/dL.

When serum creatinine is measured in µmol/L:

$$eC_{Cr} = \frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times Constant}{\text{Serum Creatinine (in } \mu\text{mol/L)}}$$

Where *Constant* is *1.23* for men and *1.04* for women.

6.3 Appendix C: Response Definition for CLL by the IWCLL Guidelines 2008

Parameter	CR*	PR*	PD*
Group A			
Lymphadenopathy†	None > 1.5 cm	Decrease ≥ 50%	Increase ≥ 50%
Hepatomegaly	None	Decrease ≥ 50%	Increase ≥ 50%
Splenomegaly	None	Decrease ≥ 50%	Increase ≥ 50%
Blood lymphocytes	< 4000/µL	Decrease ≥ 50% from baseline	Increase ≥ 50% over baseline
Marrow‡	Normocellular, < 30% lymphocytes, no B-lymphoid nodules Hypocellular marrow defines CRi	50% reduction in marrow infiltrate, or B-lymphoid nodules	--
Group B			
Platelet count	> 100,000/µL	> 100,000/µL or increase ≥ 50% over baseline	Decrease of ≥ 50% from baseline secondary to CLL
Hemoglobin	> 11 g/dL	> 11 g/dL or increase ≥ 50% over baseline	Decrease of > 2 g/dL from baseline secondary to CLL
Neutrophils‡	> 1500/µL	> 1500/µL or > 50% improvement over baseline	

Group A criteria define the tumor load, group B criteria define the function of the hematopoietic system (or marrow).
*CR (complete remission): all of the criteria have to be met, and patients have to lack disease-related constitutional symptoms; PR (partial remission): at least two of the criteria of group A plus one of the criteria of group B have to be met; SD is absence of progressive disease (PD) and failure to achieve at least a PR; PD: at least one of the above criteria of group A or group B has to be met.
CRi: complete response with incomplete marrow recovery
†Sum of the products of multiple lymph nodes (as evaluated by CT scans in clinical trials, or by physical examination in general practice).
‡These parameters are irrelevant for some response categories.

The World Health Organization (WHO) classification of hematopoietic neoplasias describes CLL as leukemic, lymphocytic lymphoma, being only distinguishable from SLL by its leukemic appearance. In the WHO classification, CLL is always a disease of neoplastic B cells, whereas the entity formerly described as chronic lymphocytic leukemia of T-cell type (T-CLL) is now called T-cell prolymphocytic leukemia. It is important to verify that the patient has CLL and not some other lymphoproliferative disease that can masquerade as CLL, such as hairy cell leukemia, or leukemic manifestations of mantle cell lymphoma, marginal zone lymphoma, splenic marginal zone lymphoma with circulating villous lymphocytes, or follicular lymphoma. To achieve this, it is essential to evaluate the blood count, blood smear, and the immune phenotype of the circulating lymphoid cells.

Blood. The diagnosis of CLL requires the presence of at least 5 x 10^9 B lymphocytes/L (5000/µL) in the peripheral blood. The clonality of the circulating B lymphocytes needs to be confirmed by flow cytometry. The leukemia cells found in the blood smear are characteristically small, mature lymphocytes with a narrow border of cytoplasm and a dense nucleus lacking discernible nucleoli and having partially aggregated chromatin. These cells may be found admixed with larger or atypical cells, cleaved cells, or prolymphocytes, which may comprise up to 55% of the blood lymphocytes. Finding prolymphocytes in excess of this percentage would favor a diagnosis of prolymphocytic leukemia (B-cell PLL). Gumprecht nuclear shadows, or smudge cells, found as cell debris, are other characteristic morphologic features found in CLL.

CLL or SLL might be suspected in otherwise healthy adults who have an absolute increase in the clonal B lymphocytes but who have less than 5 x 10^9/L B lymphocytes in the blood. However, in the absence of lymphadenopathy or organomegaly (as defined by physical examination or CT scans), cytopenias, or disease-related symptoms, the presence of fewer than 5 x 10^9 B lymphocytes per liter of blood is defined as "monoclonal B-lymphocytosis." Monoclonal B-lymphocytosis may progress to frank CLL at a rate of 1% to 2% per year.
The definition of SLL requires the presence of lymphadenopathy and/or splenomegaly. Moreover, the number of B lymphocytes in the peripheral blood should not exceed 5 x 10^9/L. In SLL, the diagnosis should be confirmed by histopathologic evaluation of a lymph node biopsy whenever possible.

Immunophenotype. CLL cells coexpress the T-cell antigen CD5 and B-cell surface antigens CD19, CD20, and CD23. The levels of surface immunoglobulin, CD20, and CD79b are characteristically low compared with those found on normal B cells. Each clone of leukemia cells is restricted to expression of either kappa or lambda immunoglobulin light chains.
Variations of the intensity of expression of these markers may exist and do not prevent inclusion of a patient in clinical trials for CLL. In contrast, B-cell PLL cells do not express CD5 in half of the cases, and typically express high levels of CD20 and surface Ig. In addition, the leukemia cells of mantle cell lymphoma, despite also expressing B-cell surface antigens and CD5, generally do not express CD23.

Marrow examination. A marrow aspirate and biopsy generally are not required for the diagnosis of CLL. In CLL, characteristically more than 30% of the nucleated cells in the aspirate are lymphoid.

From: Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute – Working Group 1996 guidelines. Blood. 2008;111(12):5446-56.

6.4 Appendix D: Criteria for B-Symptoms

Criteria for B-Symptoms

The presence of:

a) unintentional weight loss of more than 10% within the previous 6 months and/or
b) fevers of greater than 100.5°F or 38.0°C for at least 3 consecutive days without other evidence of infection and/or
c) drenching night sweats without evidence of infection is denoted by the suffix letter '**B**'. '**A**' indicates the absence of these symptoms.

6.5 Appendix E: ECOG Performance Status

Grade	Description
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 house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

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