STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Randomized, Controlled Study Evaluating the Efficacy and Safety of Idelalisib (GS-1101) in Combination with Ofatumumab for Previously Treated Chronic Lymphocytic Leukemia
Name of Test Drug:	Idelalisib (IDELA; GS-1101)
Study Number:	GS-US-312-0119
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CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALC	absolute lymphocyte count
ALT	alanine aminotransferase
ANC	absolute neutrophil count
ATC	Anatomical-Therapeutic-Chemical classification system for drugs
BID	twice per day
BMI	body mass index
BOR	best overall response
CI	confidence interval
CIRS	Cumulative Illness Rating Scale
CLL	chronic lymphocytic leukemia
CR	complete response
CT	computerized tomography
CTCAE	Common Terminology Criteria for Adverse Events
DMC	data monitoring committee
DOR	duration of response
DSPH	Gilead Sciences Department of Safety and Public Health
eCRF	electronic case report form
ECG	electrocardiogram
EQ-5D	EuroQoL Five-Dimension utility measure
EWB	Emotional Well-Being
FACT-Leu	Functional Assessment of Cancer Therapy: Leukemia questionnaire
FWB	Functional Well-Being
HLGT	high-level group term
HLT	high-level term
HRQL	health-related quality of life
Ig	immunoglobulin (including subtypes A, E, G, and M)
IgHV	immunoglobulin heavy chain variable region
IRB	institutional review board
IRC	independent review committee
ITT	intent to treat
IWCLL	International Workshop on CLL
IWRS	interactive web response system
JAK	Janus kinase
LD	longest diameter
LLN	lower limit of normal
LLT	low level term
LVD	Longest Vertical Dimension

LISTOF ABBREVIATIONS (CONTINUED)

MST	Medical Search Term
MRI	magnetic resonance imaging
ND	no disease
NE	non evaluable
ORR	overall response rate
OS	overall survival
PD	progressive disease
PK	pharmacokinetic
PI3K	phosphatidylinositol 3-kinase
PI3Kδ	phosphatidylinositol 3-kinase p110δ isoform
PFS	progression-free survival
PPD	product of the perpendicular diameters
PP	per protocol
PRO	patient-reported outcome
PR	partial response
PT	preferred time
PWB	Physical Well-Being
QTc	QT interval corrected
QTc-B	QT interval corrected for heart rate using Bazett's formula
QTc-F	QT interval corrected for heart rate using Fridericia's formula
SAE	serious adverse event
SAP	Statistical analysis plan
SD	stable disease
SPD	sum of the products of the perpendicular diameters of measured lymph nodes
SSC	study steering committee
StD	standard deviation
SUSAR	suspected, unexpected, serious adverse reaction
SWB	Social/family Well-Being
Syk	spleen tyrosine kinase
TEAE	treatment-emergent adverse event
TOI	Trial Outcome Index
TTR	time to response
ULN	upper limit of normal
WHODRUG	World Health Organization Drug Dictionary

1. INTRODUCTION

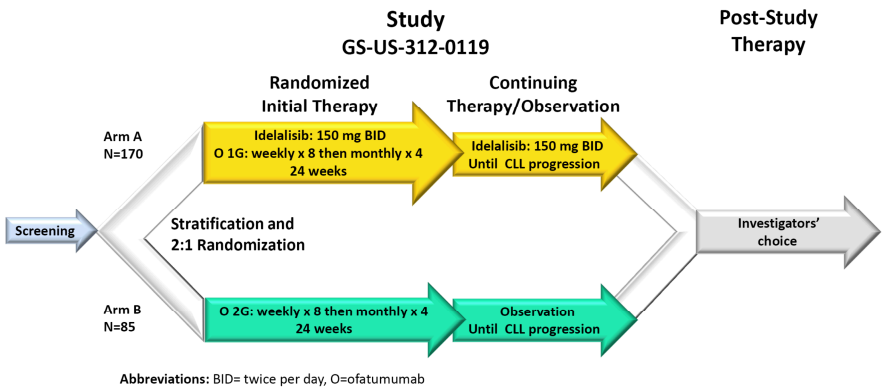
This document details the planned interim and final analyses for Study GS-US-312-0119, a Phase 3, randomized, controlled study evaluating the efficacy and safety of IDELA in combination with ofatumumab for previously treated chronic lymphocytic leukemia (CLL). Related documents are the study protocol and electronic case report form (eCRF).

1.1. Study Objectives

Primary Study Objectives	• To evaluate the effect of the addition of IDELA to ofatumumab on PFS in subjects with previously treated CLL
Secondary Study Objectives	• To evaluate the effect of the addition of IDELA to ofatumumab on the onset, magnitude, and duration of tumor control • To evaluate the effect of the addition of IDELA to ofatumumab on the onset, magnitude, and duration of tumor control for subjects with 17p deletion and/or p53 mutation • To assess the effect of the addition of IDELA to ofatumumab on measures of subject well-being, including OS, HRQL, and performance status • To assess the effects of the addition of IDELA to ofatumumab on disease-associated biomarkers and to evaluate potential mechanisms of resistance to IDELA • To characterize the effect of ofatumumab on IDELA exposure through evaluations of IDELA plasma concentrations over time • To describe the safety profile observed with the addition of IDELA to ofatumumab • To estimate health resource utilization associated with the addition of IDELA to ofatumumab

1.2. Study Design

Design Configuration and Subject Population	This study is being conducted as part of an overall clinical program that is evaluating the efficacy and safety of IDELA in the therapy of patients with previously treated CLL. Study GS-US-312-0119 is a Phase 3, multicenter, 2-arm, randomized, controlled, parallel-group study that is conducted at centers in North America, Europe and Australia.

	 Target Population: Adult subjects with previously treated recurrent CLL who have measurable lymphadenopathy, require therapy for CLL, have disease that is not refractory to ofatumumab, and might benefit from a change in therapy because they have experienced CLL progression <24 months since the completion of the last prior treatment.
Treatment Groups	• Arm A: IDELA + Ofatumumab (1000 mg) • Arm B: Ofatumumab (2000 mg)
Key Eligibility Criteria	<u>Inclusion Criteria</u> Subjects must meet all of the following inclusion criteria to be eligible for participation in this study: 1) Male or female ≥18 years of age. 2) Diagnosis of B-cell CLL, with diagnosis established according to International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria and documented within medical records. 3) CLL that warrants treatment (consistent with accepted IWCLL criteria for initiation of therapy). Any of the following conditions constitute CLL that warrants treatment: a) Evidence of progressive marrow failure as manifested by the onset or worsening of anemia and/or thrombocytopenia, or b) Massive (ie, lower edge of spleen ≥6 cm below the left costal margin), progressive, or symptomatic splenomegaly, or c) Massive (ie, ≥10 cm in the longest diameter), progressive, or symptomatic lymphadenopathy, or

	d) Progressive lymphocytosis in the absence of infection, with an increase in blood absolute lymphocyte count (ALC) ≥50% over a 2-month period or lymphocyte doubling time of <6 months (as long as initial ALC was ≥30,000/L), or e) Autoimmune anemia and/or thrombocytopenia that is poorly responsive to corticosteroids or other standard therapy, or f) Constitutional symptoms, defined as any one or more of the following disease-related symptoms or signs occurring in the absence of evidence of infection: i) Unintentional weight loss of ≥10% within the previous 6 months, or ii) Significant fatigue (≥Grade 2), or iii) Fevers >100.5°F or 38.0°C for ≥2 weeks, or iv) Night sweats for >1 month. 4) Presence of measurable lymphadenopathy (defined as the presence of ≥1 nodal lesion that measures ≥2.0 cm in the longest diameter [LD] and ≥1.0 cm in the longest perpendicular diameter [LPD] as assessed by computed tomography [CT] or magnetic resonance imaging [MRI]). 5) Prior treatment for CLL comprising therapy with either of the following types of drugs given alone or in combination: a) A purine analog (eg, fludarabine, pentostatin, cladribine) administered for ≥2 cycles of treatment b) Bendamustine administered for ≥2 cycles of treatment ***Note: Prior drugs may have been administered as single agents or as components of combination therapies. Subjects may also have received other commercially available therapies (eg, rituximab, alemtuzumab, ofatumumab, lenalidomide, corticosteroids, or others) or non-excluded investigational therapies. Each repeated but separated therapeutic application of the same single-agent or combination is considered an independent regimen.*** 6) Documentation of CLL progression <24 months since the completion of the last prior therapy for CLL. 7) Discontinuation of all therapy (including radiotherapy, chemotherapy, immunotherapy, or investigational therapy) for the treatment of CLL ≥6 weeks before randomization. ***Note: Subjects may be receiving corticosteroids to manage CLL manifestations.***

8) All acute toxic effects of any prior antitumor therapy resolved to Grade ≤1 before randomization (with the exception of alopecia [Grade 1 or 2 permitted], neurotoxicity [Grade 1 or 2 permitted], or bone marrow parameters [any of Grade 1, 2, 3, or 4 permitted]).

9) Karnofsky performance score of ≥60.

10) Required baseline laboratory data (within 4 weeks prior to randomization) as shown in the table below.
Note: Confirmation should be considered for out-of-range values to determine if the abnormality is real or artifactual. Values should be obtained within the screening period and should generally be the most recent measurement obtained. Subjects with any degree of neutropenia, thrombocytopenia, or anemia due to CLL or prior therapy may enroll.

Required Screening Laboratory Values

Organ System	Parameter	Required Value
Hepatic	Serum total bilirubin	≤1.5 x ULN (unless elevated due to Gilbert syndrome or hemolysis)
	Serum ALT	≤2.5 x ULN
	Serum AST	
Renal	eC_{Cr}[a]	>30 ml/min
Pregnancy	β-HCG[b]	Negative
Infection	HIV	Negative HIV antibody
	HBV	Negative HBsAg and negative HBc antibody or positive HBc and negative for HBV DNA by quantitative PCR
	HCV	Negative viral RNA (if HCV antibody is positive)

a As calculated by the Cockcroft-Gault formula {2202}

b For women of child-bearing potential only; serum β-HCG must be negative during screening and serum β-HCG or urine dipstick pregnancy test must be negative at randomization (Visit 2)

Abbreviations: β-HCG= beta human chorionic gonadotropin, ALT=alanine aminotransferase, AST=aspartate aminotransferase, DNA=deoxyribonucleic acid, eCCr=estimated creatinine clearance, HBc antibody=anti-hepatitis B core antibody, HBsAg=hepatitis B surface antigen, HBV=hepatitis B virus, HCV=hepatitis C virus, HIV=human immunodeficiency virus, Ig=immunoglobulin, PCR=polymerase chain reaction, RNA=ribonucleic acid, ULN=upper limit of normal

	11) For female subjects of child-bearing potential, willingness to use a protocol-recommended method of contraception from the screening visit (Visit 1) throughout the study, and for 30 days from the last dose of study drug or 12 months from the last dose of ofatumumab (whichever is later). ***Note: A female subject is considered to be of child-bearing potential unless she has had a hysterectomy, bilateral tubal ligation, or bilateral oophorectomy; has medically documented ovarian failure (with serum estradiol and follicle-stimulating hormone [FSH] levels within the institutional postmenopausal range and a negative serum or urine βHCG); or is menopausal (age ≥55 years with amenorrhea for ≥6 months).*** 12) For male subjects of child-bearing potential having intercourse with females of child-bearing potential, willingness to use a protocol-recommended method of contraception from the randomization visit (Visit 2) throughout the study and for 90 days following the last dose of study drug and to refrain from sperm donation from randomization (Visit 2) throughout the study and for 90 days following the last dose of study drug. ***Note: A male subject is considered able to father a child unless he has had a bilateral vasectomy with documented aspermia or a bilateral orchiectomy, or has ongoing testicular suppression with a depot luteinizing hormone-releasing hormone (LH-RH) agonist (eg, goserelin acetate [Zoladex®]), leuprolide acetate [Lupron®]), or triptorelin pamoate [Trelstar®]).*** 13) In the judgment of the investigator, participation in the protocol offers an acceptable benefit-to-risk ratio when considering current CLL disease status, medical condition, and the potential benefits and risks of alternative treatments for CLL. 14) Willingness and ability to comply with scheduled visits, drug administration plan, imaging studies, laboratory tests, other study procedures, and study restrictions. ***Note: Psychological, social, familial, or geographical factors that might preclude adequate study participation should be considered.*** 15) Evidence of a personally signed informed consent indicating that the subject is aware of the neoplastic nature of the disease and has been informed of the procedures to be followed, the experimental nature of the therapy, alternatives, potential benefits, possible side effects, potential risks and discomforts, and other pertinent aspects of study participation.

	Exclusion Criteria Subjects who meet any of the following exclusion criteria are not to be enrolled in this study: 1) Known histological transformation from CLL to an aggressive lymphoma (ie, Richter transformation). ***Note: Biopsy documentation of the absence or presence of transformation is not required.*** 2) Known presence of intermediate- or high-grade myelodysplastic syndrome (ie, subjects are excluded who have ≥5% bone marrow blasts; karotypic abnormalities other than normal, Y deletion, 5q deletion, or 20q deletion; or ≥2 lineages of cytopenias due to myelodysplasia). 3) History of a non-CLL malignancy except for the following: adequately treated local basal cell or squamous cell carcinoma of the skin, cervical carcinoma in situ, superficial bladder cancer, asymptomatic prostate cancer without known metastatic disease and with no requirement for therapy or requiring only hormonal therapy and with normal prostate-specific antigen for ≥1 year prior to randomization, other adequately treated Stage 1 or 2 cancer currently in complete remission, or any other cancer that has been in complete remission for ≥2 years. 4) Known hypersensitivity or intolerance to any of the active substances or excipients in the formulations for either IDELA or ofatumumab. 5) Evidence of ongoing systemic bacterial, fungal, or viral infection at the time of randomization (Visit 2). ***Note: Subjects with localized fungal infections of skin or nails are eligible. Subjects may be receiving prophylactic antiviral or antibacterial therapies at the discretion of the investigator; anti-pneumocystis prophylaxis is encouraged. For subjects who are at substantial risk of an infection (eg, influenza) that may be prevented by immunization, consideration should be given to providing the vaccine prior to initiation of protocol therapy.*** 6) Ongoing drug-induced liver injury, chronic active hepatitis C (HCV), chronic active hepatitis B (HBV), alcoholic liver disease, non-alcoholic steatohepatitis, primary biliary cirrhosis, extrahepatic obstruction caused by cholelithiasis, cirrhosis of the liver, or portal hypertension. 7) Ongoing drug-induced pneumonitis. 8) Ongoing inflammatory bowel disease.

	9) Ongoing alcohol or drug addiction. 10) Pregnancy or breastfeeding. 11) History of prior allogeneic bone marrow progenitor cell or solid organ transplantation. 12) Ongoing immunosuppressive therapy other than corticosteroids. ***Note: Subjects may use topical, enteric, inhaled, or systemic corticosteroids as therapy for manifestations of CLL, comorbid conditions, or autoimmune anemia and/or thrombocytopenia. During study participation, subjects may receive systemic or other corticosteroids as pretreatment for ofatumumab infusions or as needed for treatment-emergent comorbid conditions.*** 13) In a subject with a history of prior ofatumumab therapy, the time from the last dose of ofatumumab to documented CLL progression is <6 months. 14) History of prior therapy with any inhibitor of AKT, Bruton tyrosine kinase (BTK), Janus kinase (JAK), mammalian target of rapamycin (mTOR), phosphatidylinositol 3-kinase (PI3K) (including IDELA), or spleen tyrosine kinase (SYK). 15) Prior participation in an IDELA clinical trial. 16) Concurrent participation in another therapeutic clinical trial. 17) Prior or ongoing clinically significant illness, medical condition, surgical history, physical finding, electrocardiogram (ECG) finding, or laboratory abnormality that, in the investigator's opinion, could adversely affect the safety of the subject or impair the assessment of study results.
Study Periods/ Phases	Subjects will be randomized with a 2:1 ratio into Arm A or Arm B of the study. In Arm A, subjects will take IDELA orally BID continuously and will receive 12 infusions of ofatumumab over ~24 weeks. IDELA will be taken continuously until the earliest of subject withdrawal from study, definitive progression of CLL, intolerable study drug-related toxicity, pregnancy, substantial noncompliance with study procedures, or study discontinuation. Ofatumumab will be administered until the earliest of a maximum of 12 infusions, subject withdrawal from study, definitive progression of CLL, intolerable ofatumumab-related toxicity, pregnancy, substantial noncompliance with study procedures, or study discontinuation. Subjects in Arm A will continue with IDELA or ofatumumab, even if the other drug must be discontinued due to toxicity.

Schedule of Assessments

The schedule of assessments is located in Appendix 1 of this SAP.

Randomization and Stratification	• 2:1 allocation to Arm A vs Arm B with implementation through an interactive web response system (IWRS) • Fixed-block centralized randomization with allocation of subjects within the 8 strata as defined by the intersection of 3 binary stratification factors: — 17p deletion and/or p53 mutation in CLL cells: either vs neither (or indeterminate) — Immunoglobulin heavy chain variable region (IgHV) mutation: unmutated (or IgHV3-21) vs mutated (or indeterminate) — Disease status: refractory (CLL progression < 6 months from completion of prior therapy) vs relapsed (CLL progression ≥6 months from completion of prior therapy) There is no pre-specified limit to the number of subjects enrolled at a given site or within a stratum.
Site and/or Stratum Enrollment Limits	Approximately 115 centers in the United States, Canada, Australia, and Europe.
Study Duration	The study will continue until approximately the 129th PFS event occurs. It is expected that the study accrual period is approximately 12 months and the 129th event will occur after a minimum of 12 months of follow-up.

1.3. Sample Size and Power

Planned Sample Size	The planned sample size is 255 subjects (170 subjects in Arm A and 85 subjects in Arm B).
Power Statement	Based on data from prior studies, it is reasonable to assume that administration of ofatumumab to subjects with previously treated CLL in Arm B of this trial will result in a median PFS of ~8 months. An improvement in median PFS from 8 months to 14 months resulting from the addition of IDELA to ofatumumab in Arm A of the study would correspond to a benefit ratio of 1.75 (hazard ratio 0.57).

	It is assumed that PFS times are exponentially distributed in each of the 2 arms. With a hazard ratio (HR) equal to 1 under the null hypothesis of no difference between the 2 treatment arms and a HR of 0.57 under the alternative hypothesis of superiority of the IDELA containing combination, 129 events (definitive CLL progressions or deaths) are required to achieve a power of ~0.85 based on a log-rank test with a 2-sided significance level of 0.05. Further assuming a planned accrual period of 12 months (with approximately half of the subjects enrolled during the initial 60% of the accrual period, and the remaining half of the subjects enrolled during the last 40% of the accrual period), a minimum follow-up period of 12 months, and an expectation that 10% of subjects will be lost to follow-up (5% during the accrual period and 5% during the follow-up period) and to ensure the primary analysis on PFS will be performed before or at the planned minimum 12-month follow-up period, approximately 170 subjects will be enrolled into Arm A and approximately 85 subjects will be enrolled into Arm B. Using these assumptions, the expected number of events would be achieved by the end of the planned minimum 12-month follow-up period. It is expected that there will be approximately 65 deaths at the time of final analysis. This would provide ~ 85% power to detect a HR of 0.45 for overall survival based on a log-rank test at a 2-sided alpha level of 0.03.
Actual Enrollment and Impact on Power	The study is fully enrolled as it was originally planned and there is no impact on the power of the planned analyses.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analysis

The data monitoring committee (DMC) will have access to serious adverse events (SAEs) requiring expedited reporting and will be provided with cumulative safety data on a regular basis. An interim safety review will be conducted by the DMC at ~6 months after the first subject is enrolled. Thereafter, interim safety reviews will be performed by the DMC at intervals of ~6 months; the specific frequency of these reviews will depend upon the rate at which the trial is enrolled, the nature of any emerging safety signals, and monitoring recommendations from the DMC. At each review, all available safety data will be summarized and evaluated.

Two formal interim efficacy analyses are planned after approximately the 50% and 75% progression free survival (PFS) event has occurred. Although the study is open-label, the Gilead Sciences 312-0119 Study Team will remain blinded to any integrated summary by treatment groups throughout the trial until either the decision is made to stop the study early or all planned subjects have completed the study and the database has been locked and unblinded. The DMC will review unblinded integrated interim efficacy results and make recommendations per pre-specified efficacy boundaries to Gilead Executive Management as outlined in the DMC Charter. These analyses offer the opportunity to assess for evidence of substantial clinical benefit. For these analyses, all available PFS data will be evaluated.

Stopping the study for substantial evidence of IDELA benefit will be considered if the PFS is significantly better in Arm A (IDELA + ofatumumab) compared to Arm B (ofatumumab). The significance level for the first interim analysis will be 0.003 and for the second interim analysis will be 0.018, using the O'Brien Fleming (OF) alpha spending function. Based on the assumptions of the study and the timing of the planned analysis, boundary-crossing probabilities for the trial are provided in Table 2-1. If a decision is made to stop the trial based on an interim analysis, the database will be cleaned and locked for the subsequent final analysis the date of which will be determined in discussions with regulatory authorities, for which all the remaining alpha will be spent.

Table 2-1. The Expected Number of Events at Interim and Final Analyses and Significance Levels to Reject H_0

Analyses	Expected Number of Events[a] n (%)		Significant Level to reject H_0
Interim #1	65	(50%)	<0.003
Interim #2	97	(75%)	<0.018
Final	129	(100%)	<0.044

a Definitive CLL progressions or deaths

2.2. Final Analysis

The final efficacy analysis will be conducted after approximately 129 events (definitive CLL progression or death) or ~15 months after last subjected enrolled, whichever occurs first, unless a decision is made to stop the trial early based on an interim analysis. It is expected that this number of events will occur after a minimum of 12 months of follow-up. Once outstanding data queries have been resolved, the database will be locked, and the efficacy analysis of the study will be performed. The significance level planned for the final analysis is at 0.044 but will be adjusted based on the actual number of events observed at the time of final analysis.

2.3. Follow-up Analyses

After the final analysis, additional supplemental analyses of efficacy and safety may be performed to satisfy regulatory requirements and to perform long-term efficacy, safety, and overall survival (OS) follow-up.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

3.1. Analysis Sets

3.1.1. Intent-to-Treat Analysis Set

The intent-to-treat (ITT) analysis set includes all subjects who are randomized regardless of whether subjects receive any study drug(s), or receive a different regimen from the regimen they were randomized to. Treatment assignment will be designated according to randomization.

This analysis set will be used in the analyses of subject characteristics, PFS, overall response rate (ORR), OS, lymph node response (LNR) rate, complete response (CR) rate, and health outcome variables. The analysis of PFS based on the ITT analysis set will be considered primary. Subjects in the ITT analysis set who do not have sufficient baseline or on-study tumor status information to be adequately assessed for response status will be included in the denominators in the calculation of ORR and CR rate.

3.1.2. Per-Protocol Analysis Set

The per-protocol (PP) analysis set includes data from subjects in the ITT analysis set who meet the general criteria defining the target population for this study, are adherent to the protocol, are compliant with study drug treatment, and are evaluable for relevant efficacy endpoints. Study drug assignment will be designated according to the actual treatment received. Subjects who meet any of the following criteria may be excluded from this analysis set:

- Do not have documented diagnosis of CLL within medical records during the time course of disease

- Do not have measurable lymphadenopathy (defined as the presence of ≥1 nodal lesion that measures ≥2.0 cm in the longest diameter [LD] and ≥1.0 cm in the longest perpendicular diameter [LPD] as assessed by computed tomography [CT] or magnetic resonance imaging [MRI]) at baseline as determined by the independent review committee (IRC)

- No documentation of CLL progression in < 24 months since the completion of the last prior treatment for CLL

- Known histological transformation from CLL to an aggressive lymphoma (ie, Richter transformation)

- Prior treatment for CLL not comprising any of the following:

  A) A purine analog (eg, fludarabine, pentostatin, cladribine) administered for ≥2 cycles of treatment

  B) Bendamustine administered for ≥2 cycles of treatment

- Prior therapy with any inhibitor of AKT, Bruton tyrosine kinase (BTK), Janus kinase (JAK), mammalian target of rapamycin (mTOR), phosphatidylinositol 3 kinase (PI3K) (including IDELA), or spleen tyrosine kinase (SYK).

- Karnofsky performance score of <60 at screening

- In a subject with a history of prior ofatumumab therapy, the time from the last dose of ofatumumab to documented CLL progression is < 6 months.

- Do not receive study treatment

- Adherence with study drug of <75% for subjects in arm A.

- Non-evaluable (ie, do not have a PFS event [definitive disease progression or death], and no baseline or on-study disease evaluations)

The specific classification of subjects to be excluded in the PP analysis set will be finalized prior to database lock.

The PP analysis set will be used in sensitivity analyses of the primary and following efficacy endpoints: PFS, ORR, LNR rate, duration of response (DOR), Time to Response (TTR), and CR rate.

3.2. Safety Analysis Set

A safety analysis set will include data from subjects who receive ≥1 dose of study treatment, with treatment assignments designated according to the actual treatment received.

This analysis set will be used in the analyses of safety variables as well as study treatment administration (for IDELA and ofatumumab).

3.2.1. Pharmacokinetic/ Pharmacodynamic Analysis Sets

The pharmacokinetic/pharmacodynamic (PK/PD) analysis sets include data from subjects in the safety analysis set who have the necessary baseline and on-study measurements to provide interpretable results for the specific parameters of interest.

These analysis sets will be used in the analyses of AKT phosphorylation, chemokines/cytokines, and IDELA plasma concentrations.

3.3. Strata and Covariates

Subjects will be stratified to receive study treatment via IWRS based on the following stratification factors:

- 17p deletion and/or p53 mutation in CLL cells: either vs neither (or indeterminate)
- Immunoglobulin heavy chain variable region (IgHV) mutation: unmutated (or IgHV3-21) vs mutated (or indeterminate)
- Disease status : refractory (CLL progression < 6 months from completion of prior therapy) vs relapsed (CLL progression ≥ 6 months from completion of prior therapy)

For subjects with discrepancies between the stratification factor values at randomization (ie, according to IWRS) and the actual values as documented in the eCRF, the actual strata information will be used in the analyses.

Analyses will be adjusted for the randomization strata. In the situation that there is insufficient information in a stratum (ie, if there are <6 subjects or there is no informative event in a stratum), that stratum will be pooled with the smallest adjacent stratum for stratified analyses; the smallest stratum is defined as that stratum having the fewest number of subjects or the fewest number of events in case the former is a tie and the adjacent stratum is defined as a stratum having 2 factors of the 3 at the same level.

3.4. Examination of Subject Subsets

Primary, secondary, CCI [redacted] endpoints CCI [redacted] will be examined in the following subgroups:

- Stratification factors:
  - 17p deletion and/or p53 mutation in CLL cells: either vs neither (or indeterminate)
  - Immunoglobulin heavy chain variable region (IgHV) mutation: unmutated (or IgHV3-21) vs mutated (or indeterminate)
  - Disease status: refractory vs relapsed
- 17p deletion (Yes or No [including indeterminate])
- Gender (Male or Female)
- Age group (<65 or ≥65)
- Race (White or Non-White)

All subgroup efficacy analyses will be performed using IRC assessments if there is sufficient sample size in the subgroup.

AEs and lab abnormalities will be examined in the following subgroups:

- Gender (Male or Female)
- Age group (<65 or ≥65)
- Race (White or Non-White)

3.5. Multiple Comparisons

In the efficacy analyses, the following procedures will be implemented to preserve the overall type I error rate across the primary and secondary endpoints of the study at a 2-sided significance level of 0.05.

The primary endpoint analysis will serve as the gatekeeper for the secondary endpoint analyses, ie, the primary efficacy hypothesis must be rejected at the pre-specified significance level before the efficacy hypotheses for the secondary efficacy endpoints can be evaluated. The secondary endpoints will be the following:

- ORR
- LNR rate
- OS
- PFS in the subgroup of 17p deletion and/or p53 mutated subjects
- CR rate (if there are subjects who will respond with a CR)

If the primary hypothesis is rejected either at an interim or final analysis, the 5 secondary endpoints will be sequentially tested at the 2-sided significance level of 0.03 in the order listed above. The significant level is chosen such that the overall type I error rate of testing primary and secondary endpoints is preserved at the 2-sided 0.05 significance level. The detail is described in Appendix 2. If a null hypothesis is not rejected, formal sequential testing will be stopped and only nominal significance will be cited for the remaining secondary endpoints. Analyses and p-values will be reported for all the efficacy endpoints, including the primary endpoint, the secondary endpoints, CCI

3.6. Missing Data and Outliers

Missing Data

A missing data point for a given study visit may be due to any of the following reasons:

- A visit occurred in the window but data were not collected or were unusable
- A visit did not occur in the window
- A subject permanently discontinued from the study before reaching the window

In general, values for missing data will not be imputed unless methods for handling missing data are specified.

Missing data in Functional Assessment of Cancer Therapy: Leukemia (FACT Leu) will be handled according to the administration and scoring guidelines.

Outliers

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

3.7. Data Handling Conventions and Transformations

- By-subject listings will be created for important variables in each eCRF module, and will be presented for subjects in the ITT analysis set and sorted by subject number, visit, and time (if applicable).

- Summary tables for continuous variables will contain the following statistics: N (number in analysis set), n (number with data), mean, standard deviation (StD), median, Q1, Q3, minimum, and maximum. The same number of decimal places as in the raw data will be presented when reporting minimum and maximum, 1 more decimal place than in the raw data will be presented when reporting mean, median and 2 more decimal places than in the raw data will be presented when reporting StD.

- Summary tables for categorical variables for baseline and safety data will include: N, n, and percentage. The tables for efficacy endpoints will include standard error, and 95% confidence intervals (CIs) on the percentage, where appropriate. Unless otherwise indicated, 95% CIs for binary variables will be calculated using the binomial distribution. The denominator for the percentages will be the number of subjects in the ITT analysis set at the same stratum or total as appropriate, unless otherwise specified. Missing data will be included as a row in tables where it is appropriate. All percentages will be presented as 1-decimal point, unless otherwise specified. Percentages equal to 100 will be presented as 100% and percentages will not be presented for zero frequencies.

- Tables and figures will be displayed by visit (as appropriate) for each treatment group and total (as appropriate).

- The actual stratification factor values at randomization from electronic case report form eCRF (not the ones from IWRS) will be used in all analyses.

- Data from all sites will be pooled for all analyses.

- Analyses will be based upon the observed data unless methods for handling missing data are specified. If there is a significant degree of non-normality, analyses may be performed on log-transformed data or nonparametric tests may be applied, as appropriate.

- Unscheduled visits will only be included in listings and the best or worst post-baseline summary. Unscheduled visits will not be included in the by-visit summary tables, unless otherwise specified.

- For Kaplan-Meier estimates, the 95% CIs will be calculated using the Greenwood's formula with (complementary) log-log transformation.

3.7.1. Data Handling for Efficacy Endpoints

If there is a significant degree of non-normality for a continuous endpoint, analyses may be performed on log-transformed data or using nonparametric methods, as appropriate.

3.7.2. 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 as follows:

- A value that is 1 unit less than the limit of quantitation will be used for calculation of descriptive statistics if the data is reported in the form of "<x" (x is considered the limit of quantitation). For example, if the values are reported as <50 and <5.0, then values of 49 and 4.9 will be used for calculation of summary statistics, respectively. However, for direct bilirubin, a value of "<0.1" will be treated as 0.05 for calculation of summary statistics.

- A value that is 1 unit above the limit of quantitation will be used for calculation of descriptive statistics if the data is reported in the form of ">x" (x is considered the limit of quantitation). For example, if the values are reported as >50 and >5.0, then values of 51 and 5.1 will be used for calculation of summary statistics, respectively.

- The limit of quantitation will be used for calculation of descriptive statistics if the data is reported in the form of "≤ x" or "≥ x" (x is considered as the limit of quantitation).

3.8. Visit Windows

3.8.1. Analysis Windows

For parameters that will be summarized by visit, the nominal visit as recorded on the eCRF will be used. For parameters assessed at the end of treatment (EOT) visit, the assessment results will be assigned to the next scheduled visit where the respective data were scheduled to be collected for summary. There will be no additional analysis windowing done based on the assessment date. Unscheduled visits prior to randomization will be included for the calculation of baseline values. Unscheduled scans will be used for determination of the time-to-event and tumor response efficacy endpoints.

3.8.2. 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.
- For the EuroQol Five-Dimension (EQ-5D), if 2 values are selected for a single dimension, the value of this dimension should be treated as missing.

The following algorithm will be applied for the Functional Assessment of Cancer Therapy: Leukemia FACT-Leu:

- If 2 adjacent responses are checked, 1 of them will be picked randomly.
- All others (ie, more than 2 responses are checked or 2 non-adjacent responses are checked) are counted as missing.

4. SUBJECT DISPOSITION

4.1. Subject Enrollment

A summary of subject enrollment will be provided by treatment group. The denominator for this calculation will be the number of randomized subjects. Similarly, the number and percentage of subjects randomized in each randomization stratum will be summarized. A listing of all randomized subjects will be generated to describe site, subject number, randomization date, first treatment date, subject stratification, randomized treatment arm assignment, actual treatment arm allocation, exposure of IDELA and ofatumumab, and the reason for discontinuing study treatment. If there were discrepancies in the value used for stratification assignment between IWRS and eCRF, the value collected on the CRF will be used for this summary. A listing of subjects with randomization strata that differ from stratification factor data entered in the CRF at the time of data finalization will be provided. A by-subject listing for screening failures will be provided by screening identification (ID) in an ascending order with reasons for not being eligible for enrollment to the study.

4.2. Disposition of Subjects

Study treatment disposition and study disposition summaries will be provided by treatment group.

Study treatment disposition for IDELA and ofatumumab combination arm will present the number of subjects who:

- were randomized
- were randomized but were not treated
- were treated with study drug
- have treatment ongoing
- met the primary study endpoint at the time of study drug completion according to the investigator
- discontinued the study drug (with summary of reason for discontinuation of study drug and with summary of subjects who stay on the study after discontinuation of drug)

Study disposition will present the number of subjects who:

- were randomized
- were randomized but were not treated

- were treated with study drug
- are ongoing on the study
- discontinued the study (with summary of reason for not completing)
- met the primary study endpoint at the time of study completion according to the investigator

Study disposition will be also presented with 12 weeks intervals.

Long-term follow-up disposition will present the number of subjects who:

- entered long-term follow-up
- completed long-term follow-up (with the completion of 5-year follow-up or Death)
- are on-going with long-term follow-up
- discontinued the long-term follow-up (with summary of reasons for not completing)

A separate table will also be provided to summarize the number of subjects in the PP and PK/PD analysis sets.

The denominator for the percentages of subjects in each category will be the number of subjects in the ITT analysis set. Subjects who screen failed with the reason for screen failure and subjects who were excluded for each analysis set with reasons for exclusion will be listed.

Time to discontinuation from study will be summarized and plotted. Kaplan-Meier estimates of the median, Q1, Q3, and the number of discontinued subjects and censored subjects will be provided. Subjects who discontinued without PFS events will be categorized as having an event at the time of discontinuation. Subjects who have a PFS event or are on-going will be censored at the time of the PFS event or data cut-off, respectively.

4.3. Extent of Exposure

4.3.1. Duration of Exposure to Study Drug

Duration of exposure to IDELA will be defined as (min (last IDELA dosing date [as captured on study drug completion CRF page], data cutoff date) – first IDELA dosing date + 1), regardless of temporary interruptions in study drug administration, and will be expressed in months. Duration of exposure to IDELA will be summarized for the safety analysis set who received at least one dose of IDELA during the study using descriptive statistics and as the number and percentage of subjects exposed for at least 1 day, 2, 4, 6, and 12 months, and every 6 months thereafter.

The number of ofatumumab infusions subjects received will be summarized for the safety analysis set using descriptive statistics and the number and percentage of subjects who received at least 1, 2, 4, 6, 8, 10, and 12 ofatumumab infusions.

For on-going subjects who have not completed the IDELA dosing CRF page at the time of interim analysis, the last IDELA dosing date will be imputed with the date of data cut-off. The last available ofatumumab infusion date will be used as the last ofatumumab infusion date.

For subjects who have completed IDELA, but the day of last dose is missing, the following imputation rule will be applied:

- If day is missing but the month and year are available, then the imputed day will be the first day of the month.

4.3.2. Modification with IDELA

For subjects who have IDELA modification for subjects in Arm A, the following will be summarized and the details will be listed:

- Number and percent of subjects with dose modification
- Number and percent of subjects with dose interruption with reasons for interruption
- Number and percent of subjects who are re-challenged at the starting dose (150 mg BID) and at the reduced dose (100 mg BID).
- Number and percent of subjects who were re-escalated for subjects who are re-challenged at the reduced dose.

Continuous records of IDELA dosing from the day of first dosing day of IDELA to the last dose of IDELA including modification (interruption and reduction) will be listed. Drug accountability (dose dispense and return) records will be listed in a separate listing.

4.3.3. Adherence with IDELA

Adherence (%) with IDELA will be calculated for the subjects in Arm A:

Adherence (%) = (sum of pills dispensed minus pills returned) divided by (sum over all dosing period of [total daily pills x dosing duration]), taking into account investigator-prescribed interruption, reductions, and escalations.

Descriptive statistics for adherence along with the number and percentage of subjects belonging to adherence categories (eg, $< 75\%$ or $\geq 75\%$) will be provided.

4.4. Protocol Deviations

Protocol deviations will be categorized before database finalization by Gilead. The important (major) protocol deviations will be summarized by type of deviation in the clinical study report (CSR) based on the ITT analysis set. A listing will be provided for all important protocol deviations.

5. BASELINE DATA

5.1. Demographics and Baseline Characteristics

Demographics including gender, race, ethnicity, age (years), weight (kg), height (cm), and body mass index (BMI, kg/m^2) will be summarized for the ITT analysis set. Gender, race, ethnicity, and Karnofsky performance status will be summarized by using summary statistics for categorical variables. Age (years), weight (kg), and height (cm) will be summarized using summary statistics for continuous variables. Age will be calculated as the number of years between date of birth and date of randomization.

Age (years) = (date of randomization – date of birth+1) / 365. 25 (round down to an integer)

BMI (kg/m^2) = weight / $(height)^2$ (round to 1 decimal point)

Number and percentage of subjects <65 and ≥65 years will also be summarized. A data listing will be presented for the above demographic data.

- For date of birth, only year (not day and month) may be collected due to regulation in some countries. If day and month are missing but year is available, then the day and month will be imputed as 01 Jan.

5.2. Medical History

Total CIRS scores assessed at screening and CIRS score by organ systems will be summarized using descriptive statistics and presented by treatment group based on the ITT analysis set.

Other baseline comorbidities will also be summarized using descriptive statistics. No inferential statistics will be generated.

A by-subject listing of medical history will be provided.

5.3. Disease History

Time since diagnosis (year) will be calculated by
(Date of Randomization - Date of Diagnosis)/365.25. Time since diagnosis will be summarized by using summary statistics for a continuous variable. Disease stage at diagnosis and current disease stage will be summarized using summary statistics for a categorical variable.

The number and percent of subjects who meet the following inclusion criteria that warrants treatment for CLL at the entry of study will be summarized. The details of each category are summarized Section 1.2.

- Subjects with progressive marrow failure – Evidence of progressive marrow failure as manifested by the onset or worsening of anemia and/or thrombocytopenia

- Subjects with massive, progressive, or symptomatic splenomegaly

- Subjects with massive, progressive, or symptomatic lymphadenopathy
- Subjects with progressive lymphocytosis
- Subjects with autoimmune anemia and/or thrombocytopenia that is poorly responsive to corticosteroids or other standard therapy
- Subjects with constitutional symptoms

Subjects who meet the radiographic eligibility criteria and who have bulky lymphadenopathy criteria determined by the IRC will be summarized.

Bulky lymphadenopathy is defined in 2 ways:

- The presence of ≥1 nodal lesion that measures ≥5.0 cm in the LD.
- The presence of ≥1 nodal lesion that measures ≥10.0 cm in the LD.

5.3.1.1. Incomplete Dates

All partial dates of diagnosis and dates of last regimen will be identified, and the partial dates will be imputed as follows:

- If day and month are missing but year is available, then the imputed day and month will be 01 Jan.
- If day is missing but the month and year are available, then the imputed day will be the first day of the month.

6. EFFICACY ANALYSES

An IRC was established for this study and includes primary board-certified radiologists, a board-certified adjudicating radiologist, and an independent board-certified hematologist or oncologist to perform an independent review of response and disease progression for each subject. The review comprises of an assessment of radiographic images and prospectively defined clinical data acquired during the study according to the Gilead Protocol GS-US-312-0119 Imaging Charter. The determination of CLL response and progression will be based on standardized criteria promulgated by the International Workshop on CLL {12154}, as specifically modified for this study to reflect current recommendations which consider the mechanism of action of IDELA and similar drugs {22541}. The findings of the IRC will be considered primary for analyses of PFS and other tumor control endpoints.

6.1. Definition of the Primary Efficacy Endpoint

The primary endpoint for this study is PFS, defined as the interval from randomization to the earlier of the first documentation of definitive disease progression or death from any cause; definitive disease progression is CLL progression based on standard criteria ({12154}, {22541}) other than lymphocytosis alone.

6.2. Statistical Hypothesis for the Primary Efficacy Endpoint

H_0: HR equals to 1 between Arm A (IDELA + ofatumumab) and Arm B (ofatumumab)

H_1: HR is less than 1 (Arm A is superior to Arm B in terms of PFS)

6.3. Analysis of the Primary Efficacy Endpoint

For the primary efficacy analysis, the PFS between the 2 treatment arms will be compared based on the ITT analysis set using a stratified log-rank test, adjusted for the stratification factors used for randomization. The analysis strategy for the situation where there is insufficient information in a stratum is detailed in Section 3.3. Medians, Q1, Q3, the proportion of subjects who are progression-free at 6 months and 12 months from randomization (based on Kaplan-Meier estimates), HRs, and corresponding 95% CIs (as calculated using a Cox proportional hazards regression model) will be presented. The Kaplan-Meier curve will also be plotted.

The date of definitive CLL progression will be the time point at which progression is identified by relevant objective radiographic or clinical data per the IRC.

Data will be censored on the date of the last tumor assessment (including assessments with a not evaluable [NE] outcome) for subjects

- who do not have disease progression, or
- who do not die prior to the end of study.

Data will be censored on the date of the last tumor assessment prior to the initiation of new anti-tumor therapy (including assessments with a not evaluable [NE] outcome) for subjects who start new anti-tumor therapy prior to documented disease progression.

Data will be censored on the date of the last tumor assessment prior to ≥ 2 consecutive missing tumor assessments (including assessments with a not evaluable [NE] outcome) for subjects who have ≥ 2 consecutive missing tumor assessments before disease progression or death.

Subjects without adequate baseline tumor response evaluation will be censored on the randomization date.

To assess the robustness of the primary PFS results, the following exploratory sensitivity analyses will be performed:

- PFS will be compared between the treatment arms in the ITT analysis set using the unstratified log-rank test.
- PFS will also be compared between treatment arms in the PP analysis set using the Kaplan-Meier method and the stratified log-rank test.
- PFS will be further analyzed by censoring data from surviving, non-progressing subjects only at the last time when lack of definitive CLL progression was objectively documented.
- Worst-case sensitivity analysis will be performed in which surviving, non-progressing subjects who are lost to follow-up are categorized as having an event at the time of the last known CLL tumor status assessment if they were in Arm A and are categorized as censored at the time of the last known CLL tumor status assessment if they were in Arm B. These analyses will be performed based on the ITT analysis set using the Kaplan-Meier method and the stratified log-rank test.

The Cox regression approach will be used to explore the influences of the stratification factors, other baseline characteristics, and treatment on PFS. Beyond the stratification variables, additional baseline subject characteristics (ie, gender, age, race, number of prior therapies, disease staging, etc.) may be included as covariates, focusing on those with expected prognostic significance, particularly if these show imbalance between treatment groups. For the Cox regression modeling, a stepwise selection process will be applied to these variables to identify the final subset of relevant factors. Each prognostic factor will be preliminarily evaluated in the Cox regression model. Only the variables significant at the 0.20 level will be considered to build the multivariate model. A forward selection process with significance level of 0.10 will be applied to these variables to identify the final subset of relevant factors. Once a model has been established, treatment will be added to the final subset of factors to study its effect on the model. Treatment-by-factor interactions will be explored for the subset of factors included in the final model.

To explore the potential impact for any imbalance due to different rates of drop-out between treatment groups, inverse probability of censoring weights (IPCW) {30871} with various covariates including stratification factors, and time varying covariates will be used to investigate the robustness of the primary PFS analysis.

6.4. Additional Analysis of the Primary Efficacy Endpoint

For subjects with disease progression, the reasons for PD (which criteria were met) will be summarized. Subjects who were assessed by the IRC as having PD on the basis of 1, 2, or 3 criteria will be listed and summarized by treatment arm.

The following disease progression criteria will be included:

- Progression based on index lesion
  - Increase from the nadir by ≥50% in the SPD of index lesions
  - A new node that measures >1.5 cm in the LD and >1.0 cm in the LPD
  - Increase from the nadir by ≥50% in the LD of an individual node
- Progression based on non-index lesion
  - Unequivocal increase in the size of non-index disease
- Progression based on hepatomegaly
  - New hepatomegaly
  - Recurrent splenomegaly, with a minimum longest vertical dimension (LVD) of 140 mm and a minimum increase from the nadir (if there is splenomegaly at nadir) of ≥ 50% in the size of the enlargement
- Progression based on splenomegaly
  - New splenomegaly
  - Recurrent splenomegaly, with a minimum LVD of 140 mm and a minimum increase from the nadir (if there is splenomegaly at nadir) of ≥ 50% in the size of the enlargement
- Progression based on hematological parameters confirmed by bone marrow
  - The current platelet count is <100 x 10^9/L and there has been a decrease by >50% from the highest on-study platelet count with confirmation from a bone marrow result
  - The current hemoglobin is <110 g/L (11.0 g/dL) and there has been a decrease by >20 g/L (2 g/dL) from the highest on-study hemoglobin with confirmation from a bone marrow result
- Transformation to a more aggressive histology

6.5. Secondary Efficacy Endpoints

6.5.1. Definition of Secondary Efficacy Endpoints

Secondary efficacy endpoints include:

- ORR – defined as the proportion of subjects who achieve a CR or PR and maintain their response for at least 8 weeks (with a 1-week window)
- LNR rate – defined as the proportion of subjects who achieve a ≥50% decrease from baseline in the SPD of index lesions per IRC assessments
- OS – defined as the interval from randomization to death from any cause during the study
- PFS in the subgroup of subjects with 17p deletion and/or p53 mutation - defined as the interval from randomization to the earlier of the first documentation of definitive disease progression or death from any cause
- CR rate – defined as the proportion of subjects who achieve a CR and maintain their response for at least 8 weeks (with a 1-week window)

To preserve the overall type I error rate across the primary and secondary endpoints of the study at a 2-sided significance level of 0.05, the primary efficacy hypothesis must be rejected at the pre-specified significance level before the efficacy hypotheses for the secondary efficacy endpoints can be tested. The 5 secondary endpoints will be sequentially tested at the 2-sided 0.03 significance level in the order listed above. The significant level is chosen in such a way that the overall type I error rate of testing primary and secondary endpoints are preserved at the 2-sided 0.05 significance level in this group-sequential designed study. The detail is described in Appendix 2. If a null hypothesis is not rejected, formal sequential testing will be stopped and only nominal p-value will be cited for the remaining secondary endpoints.

6.5.2. Analysis Methods for Secondary Efficacy Endpoints

Responses will be categorized as CR, PR, stable disease (SD), or PD. For subjects who initially responded but did not have an evaluable follow up visit or did not maintain a response (ie, progressed) for at least 8 weeks (with a 1-week window) will be categorized as having a SD. In addition, a response category of NE is provided for situations in which there is inadequate information to otherwise categorize response status. A response category of no disease (ND) is included for situations in which there is no evidence of tumor either at baseline or on treatment.

6.5.2.1. Overall response rate

ORR is defined as the proportion of subjects who achieve a CR or PR during the study and maintain the response for at least 8 weeks (with a 1-week window). Differences in number and percentage of subjects between the treatment arms in ORR will be compared using CMH Chi-square tests after adjusting for stratification factors. Odds ratios and the corresponding 95% CIs will be presented as well.

The potential influence of subject baseline characteristics (gender, age, race, number of prior therapies, disease staging, etc.), and of treatment on response rates will be explored with logistic regression modeling. For the regression modeling, a stepwise selection process will be applied to these variables to identify the final subset of relevant factors. Each prognostic factor will be preliminarily evaluated in the logistic regression model separately. Only the variables significant at the 0.20 level will be considered to build the multivariate model. A forward selection process with significance level of 0.10 will be applied to these variables to identify the final subset of relevant factors. Once a model has been established, treatment will be added to the final subset of factors to study its effect on the model. Treatment-by-factor interactions will be explored for the subset of factors included in the final model.

The primary ORR analysis will be evaluated using the IRC assessments based on the ITT analysis set. Sensitivity analyses will be performed using the IRC assessments based on the PP analysis set, and defining ORR as the proportion of subjects who achieve a CR or PR during the study.

Investigators assessments with 8 weeks (with a 1-week window) confirmation will also be used for ORR analysis. Consistency of evaluation between IRC and investigator assessments in each treatment arm will be summarized by the percent agreement for overall response

6.5.2.2. Lymph node response rate

Differences in LNR between the 2 treatment arms will be compared using CMH Chi-square tests after adjusting for stratification factors. Only subjects that have both baseline and ≥1 evaluable post-baseline SPD will be included for this analysis. Logistic regression for lymph node response rate will be performed in a similar fashion that is described in Section 6.5.2.1.

6.5.2.3. Overall Survival

The OS analysis will be performed using the ITT analysis set (according to the original randomization) which includes all available survival information during the study with long-term follow-up to the data cut-off date. Data from surviving subjects will be censored at the last time that the subject was known to be alive on study (including all the in-person visit dates captured in the datasets, ie, BM biopsy, central lab collection, CT scan, physical exam, drug administration in clinic, concomitant medication and therapy start date, ECG, PRO collection, long term follow up, hospitalization, transfusion, pregnancy testing). Differences between treatment arms in OS will be assessed in the ITT analysis set using a stratified log rank test, adjusted for the stratification factors. Plots of time to event by treatment arm will be done using the Kaplan-Meier method. Medians, Q1, Q3, ranges, HRs, and corresponding 95% CIs will be presented by treatment arm.

A supportive Cox regression analysis of OS in the ITT analysis set will be performed using the same methods as in the analysis of PFS (Section 6.3) if a sufficient number of events occur.

6.5.2.4. PFS in the subgroup of 17p deletion and/or p53 mutated subjects

Details of PFS analysis is described in Section 6.3. PFS between the 2 treatment arms will be compared based on the ITT set with the subgroup of subjects with 17p deletion and/or p53 mutation using unstratified log-rank test.

6.5.2.5. Complete Response Rate

The same analyses as specified for ORR in Section 6.5.2.1 will be performed for the CR rate. A sensitivity analysis of CR rate will be performed by assigning subjects without a confirmed response of CR to the initial response of CR.

6.6. Exploratory Efficacy Endpoints

6.6.1. Definition of Exploratory Efficacy Endpoints

CCI

[redacted]

6.6.2. Analysis Methods for Exploratory Efficacy Endpoints

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CCI [redacted]

6.7. Changes From Protocol-Specified Efficacy Analyses

By the time of the data cut specified for the first interim analysis (50% PFS events), the actual number of PFS events was close to the number of PFS events targeted for the second interim (75% PFS events). Therefore, per the OF alpha spending function, the alpha level 0.018 will be used for this first interim analysis and there will be no second interim analysis.

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

The focus of AE summarization will be on treatment-emergent AEs (TEAEs). All AEs and deaths occurring on study will be summarized by treatment arm and listed in detail based on the safety analysis set.

7.1.1. Adverse Event Dictionary

AEs will be coded using the current Medical Dictionary for Regulatory Activities (MedDRA) by system organ class (SOC), high level group term (HLGT), high level term (HLT), preferred term (PT), and lower level term (LLT).

7.1.2. Adverse Event Severity

The severity of AEs will be graded by the investigator according to the CTCAE, Version 4.03, whenever possible. If a CTCAE criterion does not exist, the grade corresponding to the appropriate adjective used by the investigator to describe the maximum intensity of the AE. The severity grade will be categorized as:

- Grade 1 (mild)
- Grade 2 (moderate)
- Grade 3 (severe)
- Grade 4 (life threatening), or
- Grade 5 (fatal)

A missing severity grade will be considered as missing.

7.1.3. Relationship of Adverse Events to Study Drug

The relationship of an AE to the component of study drug (IDELA) and ofatumumab and to the infusion of ofatumumab should be assessed by the investigator using clinical judgment, describing the event as either unrelated or related. Events for which the investigator did not record relationship to study drug and ofatumumab will be considered related to study drug and ofatumumab. Data listings will show relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) are those identified as serious in the clinical database. The clinical database will be reconciled with the SAE database from the Drug Safety and Public Health Department before database finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent

TEAEs are events in a given study period that meet one of the following criteria:

- Events with onset dates on or after the start of treatment and up to 30 days after the permanent discontinuation of the study treatment.
- AEs resulting in treatment discontinuation after the start of treatment.

7.1.5.2. Incomplete Dates

All AEs with partial onset or stop dates will be identified and the partial dates will be imputed as follows:

- For AE onset date: If day and month are missing but year is available, then the imputed day and month will be 01Jan or the first dosing date if they have the same year, 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 first dosing date if they have the same month and year, whichever is later.
- For AE stop date: If day and month are missing but year is available, then the imputed day and month will be 31Dec or 30 days after the last dose of study treatment (ie, ofatumumab or IDELA) if they have the same year, whichever is earlier. If day is missing but the month and year are available, then the imputed day will be the last day of the month or 30 days after the last dose of study treatment if they have the same month and year, whichever is earlier.

7.1.6. Summaries of Adverse Events and Deaths

A brief summary of TEAEs by treatment arms (or for the relevant treatment arm) will show the number and percentage of subjects who (1) had any AE, (2) had any Grade ≥3 AE, (3) had any IDELA-related AE, (4) had any ofatumumab -related AE, (5) had any Grade ≥3 IDELA-related AE, (6) had any Grade ≥3 ofatumumab -related AE, (7) had any SAE, (8) had any IDELA-related SAE, (9) had any ofatumumab -related SAE (10) discontinued from study drug due to an AE, (11) dose interruption or modification due to an AE, (12) death due to AEs (10) on-study deaths and (13) all deaths including long-term follow up.

Summaries (number and percentage of subjects) of TEAEs (by SOC, HLT, and PT) will be provided by treatment arms (or for the relevant treatment arm) using the safety analysis set as follows:

- AEs
- AEs by CTCAE Grade
- Grade ≥3 AE
- IDELA related AEs
- Ofatumumab related AEs
- Infusion related AEs based on PT and based on Gilead medical search terms (MST) list
- SAEs
- IDELA and ofatumumab related SAEs
- AEs leading to IDELA reduction and/or interruption
- AEs leading to IDELA interruption
- AEs leading to IDELA reduction
- AEs leading to ofatumumab delay
- AEs leading to discontinuation from IDELA
- AEs leading to discontinuation from ofatumumab
- AEs leading to death
- All non-serious AEs occurring in at least 5% of subjects in any treatment group
- AE occurring more frequently in either treatment group by PT (Relative Risk and P-value)
- AE by Time interval (12 weeks intervals)
- AE incidence rate adjusted for Total exposure

Multiple events will be counted once only per subject in each summary. For data presentation, SOC, HLT, and PT will be sorted by decreasing frequency. For summaries by severity grade, the most severe event will be selected. In addition to the presentation by SOC and HLT, each summary will also be presented by preferred term only, ordered by decreasing frequency.

In addition, TEAE difference ≥2% (all grades) or ≥2% in Grade ≥3 between the 2 treatment arms will be summarized by PT and volcano plot for relative risk of TEAEs between the treatment arms and their p-values will be plotted.

In addition to the by-treatment summaries, data listings will be provided for the following:

- All TEAEs
- All AEs recorded between screening and first dose of study treatment (ie, non-TEAEs)
- SAEs (with a variable indicating whether the event is treatment-emergent)
- AEs leading to discontinuation of IDELA
- Deaths
- TEAE difference ≥2% (all grades) or ≥2% in Grade ≥3 between the 2 treatment arms

Relative day from first dose date will be provided for each AE in the listings. The relative day will be calculated as (AE onset date - first dose date + 1).

Incidence of TEAEs will also be summarized by time interval, 0 to <12 weeks, 12 to <24 weeks, 24 to <36 weeks, 36 to <48 weeks, and >= 48 weeks. Incidence of TEAE within the first 6 months from the first dose will be summarized. Incidence of TEAEs in an interval is defined as the proportions of subjects with TEAEs within the interval in the safety analysis set.

7.1.7. Exposure-adjusted TEAE Rate

The exposure-adjusted TEAE rate is defined as the number of subjects with a specific event divided by the total exposure-time among the subjects in the treatment group and at risk of an initial occurrence of the event. Specifically,

$$Exposure\text{-}Adjusted\ TEAE\ Rate = \frac{n}{T} = \frac{n}{\sum t_i}$$

Where n is the number of subjects with events, t_i is the i^{th} subject exposure time in weeks and T is the total exposure time in weeks of all subjects. If a subject has multiple events, the t_i is the time of the first event. For a subject with no event, the t_i will be censored at the time of data cut-off date if the subject is still on study drug; and the t_i will be censored at the time of last does date plus 30 days or data cutoff date whichever is shorter if the subject discontinues study drug.

The exposure-adjusted TEAE rate will be summarized for certain AEs of interest by treatment arm based on the safety analysis set.

7.1.8. Treatment-Emergent Adverse Events (TEAEs) of Interest

Additional analyses on AEs of interest will be performed.

The following AEs of interest will be summarized similarly to TEAE by treatment arms. AEs of interest leading to interruption and/or reduction, and leading to treatment discontinuation will be also summarized.

- **Grade ≥ 3 Rash** based on Gilead medical search list including multiple MedDRA preferred terms dermatitis exfoliative, drug eruption, rash, rash erythematous, rash generalised, rash macular, rash maculo-papular, rash papular, rash prutitic, rash morbiliform, and exfoliative rash
- **Grade ≥ 3 Diarrhea/Colitis** including diarrhea and colitis
- **Any Grade Pneumonitis**
- **Grade ≥ 3 Pneumonia** including pneumonia, lung infection, lung infiltration, *pneumocystis jiroveci* pneumonia, pneumonia legionella, lung infection pseudomonal, pneumonia fungal, lower respiratory tract infection, and lower respiratory tract infection bacterial.

Number and percentage of subjects with AEs of interest will be summarized by treatment arms for subjects:

- with any grade (or Grade 3 or 4) AEs of interest
- re-challenged after dose interruption due to AEs of interest
- re-challenged successfully after interruption with resumption of IDELA at a starting dose
- re-challenged successfully after interruption with resumption of IDELA at a reduced dose
- with recurrence of AEs of interest among re-challenged

Incidence of AEs of interest (of any grade and Grade 3 or higher) over time in 12-week intervals will be summarized and plotted. Incidence of TEAEs in an interval is defined as the proportion of subjects with onset of the TEAE in the interval among those at risk at the beginning of the interval. The incidence over time describes the risk (constant or changing) of developing a new or recurrent event over time. The subjects at risk include those on treatment or within 30 days post last dose date for subjects who didn't die at the beginning of the interval.

Prevalence of AEs of interest (of any grade and Grade 3 or higher) over time in 12-week intervals will be summarized and plotted. Prevalence of TEAEs is defined as the proportion of subjects experiencing a TEAE in the interval among those at risk at the beginning of the interval. The prevalence over time describes the risk (constant or changing) of having an event over time. The subjects at risk include those on treatment or within 30 days post last dose date for subjects who didn't die at the beginning of the interval.

The following analyses of time to onset and time to resolution will be done for pneumonitis and diarrhea/colitis.

Time to first onset of AE of interest (of any grade and Grade 3 or higher) and time to resolution will be summarized and plotted. Kaplan-Meier estimates of the median, Q1, Q3, and the number of subjects with event and censored subjects will be provided.

Time to onset of first event is defined as time from start of study treatment to the date of first incident treatment-emergent AEs of interest, ie, time in weeks is calculated as (start date of first occurrence – date of first dose of study drug +1)/7. In the absence of an event, the censoring date applied will be the earliest from the following dates: last dose date (if treatment discontinued or 12 doses of ofatumumab is completed for Arm B subjects) + 30 days, analysis data cut-off date and death date. Time to resolution of AE of interest is calculated as (AE resolution date - start date of first occurrence of AE +1)/7.

7.2. Laboratory Evaluations

Summaries of laboratory data (including hematology, serum chemistry, and selected immunoglobulin parameters) will be provided for the safety analysis set. All laboratory data will be listed. Summaries of laboratory data will be based on observed data and will be reported using SI units. The focus of laboratory data summarization will be on treatment-emergent laboratory abnormalities using the safety analysis set.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics (sample size, mean, StD, median, Q1, Q3, minimum and maximum) will be provided for each laboratory test specified in the study protocol as follows:

- Baseline values
- Values at each post-baseline visit
- Change from baseline at each post-baseline visit

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.2. In addition, the raw values (± StD), mean change from baseline (± standard error) and median raw values (± Q1/Q3) for all lab parameters will be plotted over time by treatment arms.

7.2.2. Summaries of Categorical Laboratory Results

Laboratory data that are categorical will be summarized using number and percentage of subjects in the study with the given response at baseline and each scheduled post-dose assessment by treatment arms.

7.2.3. Graded Laboratory Values

Applicable hematological and serum biochemistry laboratory data will be programmatically graded according to CTCAE, Version 4.03 severity grade [grade laboratory results as Grade 0, mild (Grade 1), moderate (Grade 2), severe (Grade 3), or life threatening (Grade 4)]. Grade 0 includes all values that do not meet criteria for an abnormality of at least Grade 1.
Some laboratory tests have criteria for both increased and decreased levels; analyses for each direction (ie, increased, decreased) will be presented separately. Local labs will be graded based on central lab normal ranges with in-house macro. Local labs of ANC, lymphocytes, Platelet, Hemoglobin, Aspartate aminotransferase, Alanine aminotransferase, Total bilirubin, and Alkaline Phosphatase are included in the table summaries when central labs are not available. All central and local labs will be listed.

7.2.3.1. Treatment-Emergent Laboratory Abnormalities

A treatment-emergent laboratory abnormality is defined as an abnormality that, compared to baseline, worsens by ≥1 grade in the period from the first dose of study drug to 30 days after the last dose of study treatment. If baseline data are missing, then any graded abnormality (ie, an abnormality that is Grade ≥1 in severity) will be considered treatment-emergent.

7.2.3.2. Summaries of Laboratory Abnormalities

Summary (number and percentage of subjects) of baseline and worst post-baseline treatment-emergent laboratory abnormalities for treatment-emergent lab abnormalities and treatment-emergent Grade 3 or 4 lab abnormalities will be provided by treatment arms. Subjects will be categorized according to most severe abnormality grade.

For all summaries of laboratory abnormalities, the denominator is the number of subjects in the safety analysis set. A listing of treatment-emergent Grade ≥ 3 laboratory abnormalities will be provided. Lab abnormalities incidence difference ≥ 5% (all grades) or ≥ 2% in Grade ≥ 3 between 2 arms will be summarized and volcano plot for relative risk of lab abnormalities between the treatment arms and their p-values will be plotted.

7.2.3.3. Exposure-adjusted Treatment-Emergent Laboratory Abnormalities Rate

The exposure-adjusted treatment-emergent lab abnormalities will be analyzed similarly to the exposure-adjusted TEAE rates (outlined in Section 7.1.7).

7.2.4. Shift in CTCAE Grade Relative to Baseline

Shift tables will be presented by showing change in CTCAE severity grade from baseline to the worst grade post baseline.

7.2.5. Transaminase elevations

Analyses of transaminase elevations will be based on laboratory values using the safety analysis set. Number and percentage of subjects will be summarized by treatment arms for subjects:

- with Grade 3 or 4 ALT/AST elevation
- with Grade 3 or 4 ALT/AST elevation resolved to both ALT/AST of Grade 1 or less
- re-challenged after dose interruption due to Grade 3 or 4 ALT/AST elevation
- with recurrence of Grade 3 or 4 ALT/AST elevation among re-challenged
- with recurrent Grade 3 or 4 ALT/AST elevation resolved to both ALT/AST of Grade 1 or less

Kaplan-Meier curves and estimates will be provided for time to onset of first Grade 3 or 4 treatment-emergent ALT/AST elevations. Time to onset of first event is defined as time from start of study treatment to the start date of first Grade 3 or 4 treatment-emergent ALT/AST elevation, ie, time in weeks is calculated as (start date of first occurrence – date of first dose of study drug +1)/7. In the absence of an event, the censoring date applied will be the earliest from the following dates: last ALT/AST collection date, last dose date (if treatment discontinued or 12 doses of ofatumumab is completed) + 30 days, analysis data cut-off date, and death date.

For subjects with at least 1 episode of Grade 3 or 4 ALT/AST elevation, time to resolution of first episode of treatment-emergent Grade 3 or 4 ALT/AST elevation to Grade 1 or less will be summarized using Kaplan-Meier estimates. The same censoring rule described above for time to onset will be used. In addition, the same analysis will be performed for subjects who are re-challenged due to Grade 3 or 4 treatment-emergent ALT/AST elevations.

7.2.6. Liver-Related Laboratory Tests

The number and percentage of subjects will be summarized for the following liver-related laboratory tests and categories:

- Aspartate aminotransferase (AST): (a) 3 to <5 x ULN, (b) 5 to <10 x ULN, (c) 10 to <20 x ULN, (d) ≥ 20 x ULN
- Alanine aminotransferase (ALT): (a) 3 to <5 x ULN, (b) 5 to <10 x ULN, (c) 10 to <20 x ULN, (d) ≥ 20 x ULN
- AST or ALT: (a) 3 to <5 x ULN, (b) 5 to <10 x ULN, (c) 10 to <20 x ULN, (d) ≥ 20 x ULN
- Total bilirubin: (a) > ULN, (b) > 1.5 x ULN, (c) > 2 x ULN
- AST or ALT > 3 x ULN and total bilirubin > 1.5 x ULN

- AST or ALT > 3 x ULN and total bilirubin > 2 x ULN
- Alkaline Phosphatase >1.5 x ULN

For individual laboratory tests, subjects will be counted once based on the most severe post-baseline values.

Among the subjects with elevated AST or ALT (> 3 x ULN), the following 2 approaches will be used for counting subjects with total bilirubin elevation/normal alkaline phosphatase (≤1.5 x ULN):

- Subjects will be counted once when total bilirubin elevation/normal alkaline phosphatase occurred at any post-baseline visit.
- Subjects will be counted once when total bilirubin elevation/normal alkaline phosphatase occurred concurrently at the same post-baseline visit with AST or ALT elevation.

  In addition, a listing of subjects meeting each category will be provided

7.3. Prior Therapy (Including Radiation)

Number of prior regimens and time since the completion of last regimen will be summarized by treatment arms using descriptive statistics (sample size, mean, standard deviation, median, Q1, Q3, minimum and maximum) based on the safety analysis set. A partial completion date will be imputed using the following algorithm for the last regimen:

- If day and month are missing but year is available, then the imputed day and month will be 01 Jan 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.

Number (%) of subjects who received 1, 2, 3, ... prior regimens will also be provided. The regimens and prior therapies (n, %) that the subjects received will be summarized. The last regimen subjects received prior to study entry and the best response (n, %) to last therapy will be summarized.

Number of subjects who received prior radiation will be summarized and will be listed.

7.4. Concomitant Medications

Concomitant medications will be coded by means of the World Health Organization Drug (WHODRUG) dictionary, Q1 2011 into Anatomical-Therapeutic-Chemical classification (ATC) codes.

Concomitant medications are defined as any medications meeting the following criteria:

- Starting on or after the first dose of study drug up to 30 days post the last dose
- Starting before and continuing after the first dose of study drug up to 30 days post the last dose

The incomplete dates handling method used for AE summaries will be used for concomitant medication summaries (Section 7.1.5.2).

Prior medications are defined as any medications stopped before the first dose of study drug. Summaries of the number and percentage of subjects who used prior and concomitant medications will be presented in tabular form by preferred drug name based on the safety analysis set. The summary tables will be sorted by descending frequency of preferred terms. Subjects will only be counted once for multiple drug use (by preferred drug name) per subject.

Concomitant medications started on/-after the start of study medication or ongoing medications will be flagged on the prior and concomitant medication data listing.

The summaries and listings will be based on the safety analysis set.

7.5. Body Weight and Vital Signs

Body weight at each visit, and change from baseline in body weight will be summarized for the safety analysis set using descriptive statistics by treatment group for each post baseline visit. In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.2. No inferential statistics will be generated.

7.6. Electrocardiogram Results

The following analyses of electrocardiogram (ECG) results are intended to identify gross changes in QT intervals. ECG data will be categorized at the investigational sites as normal, abnormal but not clinically significant, or abnormal and clinically significant.

7.6.1. Corrected QT Intervals

Corrected QT (QTc) intervals will be derived by using Fridericia method:

Fridericia: $QTc\text{-}F = QT / (RR)^{1/3}$,

where, RR is calculated as [60 / Heart Rate (beats/min)].

The QTc data (msec) obtained by using the Fridericia correction will be categorized separately into the following classifications and summarized for screening:

- ≤ 450
- 451–480
- 481–500
- > 500

The change in QTc values (msec) obtained by using the Fridericia's correction will also be categorized separately as follows:

- ≤ 30
- 31-60
- > 60

7.6.2. Investigator Assessment of ECG Readings

The number and percentage of subjects in the safety analysis set with an investigator's ECG assessment of normal, abnormal but not clinically significant, or abnormal and clinically significant will be summarized by treatment group for screening.

7.6.3. Oxygen Saturation Levels

Oxygen percent saturation and its change from baseline will be summarized for the safety analysis set using descriptive statistics by treatment group. Summaries of oxygen saturation data will be based on observed data and will be reported as % saturation. The number and percentage of subjects who achieve the lowest value below 92% and ≥5% decrease from baseline in oxygen percent saturation will be summarized by treatment group.

7.7. Other Safety Measures

Physical examination results will be summarized by body system and visit. All results will be listed.

A data listing will be provided for subjects experiencing pregnancy during the study.

7.8. Changes From Protocol-Specified Safety Analyses

Not applicable.

8. PHARMACOKINETIC ANALYSES

Bioanalytical analyses will performed independently so that the study team and investigators will not have knowledge of data from individual subjects. For Arm A, the IDELA plasma concentrations immediately pre-dose and at 1.5 hours after administration of the dose of study drug at each relevant clinic visit will be summarized by treatment and visit using descriptive statistics.

9. PHARMACODYNAMIC ANALYSES

A separate biomarker analysis plan will be prepared to detail pharmacodynamics and biomarker analyses.

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11. SOFTWARE

SAS® Software Version 9.2. SAS Institute Inc., Cary, NC, USA.

12. SAP REVISION

Revision Date (dd month, yyyy)	Section	Summary of Revision	Reason for Revision
25Sep2014	6.7	Change in alpha level for the interim analysis	See section 6.7

13. APPENDICES

Appendix 1. Schedule of Assessments

Period	Screen	Treatment																		Follow-up	
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18+**			
Week	**-4**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**12**	**16**	**20**	**24**	**30**	**36**	**42**	**48**			**30 day**	**Long-term**
Study Day	**Within -28 Days**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**78**	**106**	**134**	**162**	**204**	**246**	**288**	**330**	**Q12 Weeks**	**End of Study**	**Within +30 days**	**To +5 years**
Visit Window			**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±7**			
Informed consent	X																				
Medical history	X																				
CIRS assessment	X																				
Serum virology	X																				
β-HCG (women of child-bearing potential)	X	X				X			X	X	X	X	X	X	X	X	X[a]	X[a]	X		
CLL peripheral blood evaluation	X																		X		
CLL serology	X																		X		
Coagulation	X																				
Urinalysis	X																				
12-lead ECG	X																				
Genotyping and expression analysis		X																	X		
IWRS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

Period	**Screen**	**Treatment**																		**Follow-up**	
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18+**			
Week	**-4**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**12**	**16**	**20**	**24**	**30**	**36**	**42**	**48**			**30 day**	**Long-term**
Study Day	**Within -28 Days**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**78**	**106**	**134**	**162**	**204**	**246**	**288**	**330**	**Q12 Weeks**	**End of Study**	**Within +30 days**	**To +5 years**
Visit Window			**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±7**			
HRQL/healthy utility – FACT-Leu/EQ-5D		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Performance status	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Oxygen saturation (by pulse oximetry)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Physical exam (includes nodes, liver, spleen)	X	X				X			X	X	X	X	X	X	X	X	X	X	X		
Hematology/ serum chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Circulating cells/biomarkers/serum Igs		X	X	X		X			X	X	X	X	X	X	X	X	X	X	X		
Idelalisib administration in clinic (Arm A only)		X		X		X			X	X			X								

Period	Screen	Treatment																		Follow-up	
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18+**			
Week	**-4**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**12**	**16**	**20**	**24**	**30**	**36**	**42**	**48**			**30 day**	**Long-term**
Study Day	**Within -28 Days**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**78**	**106**	**134**	**162**	**204**	**246**	**288**	**330**	**Q12 Weeks**	**End of Study**	**Within +30 days**	**To +5 years**
Visit Window			**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±2**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±7**			
Premedication and ofatumumab administration		X	X	X	X	X	X	X	X	X	X	X	X								
Infusion reaction severity/ duration assessment		X	X	X	X	X	X	X	X	X	X	X	X								
Idelalisib pharmacokinetics (Arm A only)		X		X		X			X	X			X								
Idelalisib dispensing/accounting (Arm A only)		X								X			X		X		X	X	X		
Radiology assessment (CT/MRI) [b]	X								X		X		X		X		X	X	X		
Bone marrow biopsy/ aspirate[c]	X								X		X		X		X		X	X			
HBV DNA by PCR[d]						X			X	X	X	X	X		X		X	X			
Post-study CLL therapy																					X
Long-term follow-up																					X

a After Visit 17 and 18, urine β-HCG to be performed every 6 weeks ±5 d (women of child-bearing potential only)
b At screening, CT/ MRI may be performed within 6 weeks prior to start of randomization); CT or MRI imaging of neck, chest, abdomen, and pelvis can be performed within 1 week of the visit. CT/MRI assessments will continue until ~129 events have been observed in the study population

c At baseline, to be performed at investigator discretion to determine extent of CLL involvement and bone marrow cellularity. Post-baseline, to confirm CR or PD; if the subject does not otherwise meet criteria for CR or if the nature of PD does not require bone marrow confirmation, it is not necessary to obtain a follow-up bone marrow biopsy/aspirate.

d Only subjects who are HBc antibody positive and HBV DNA negative at screening. Subjects will be tested monthly for the duration of ofatumumab therapy and every 3 months thereafter for 1 year from the last dose of ofatumumab .

Abbreviations: β-HCG=beta human chorionic gonadotropin, CIRS=chronic illness rating scale, CLL=chronic lymphocytic leukemia, CR=complete response, CT=computed tomography, ECG=electrocardiogram, EQ-5D=EuroQoL Five-Dimension, FACT-Leu=Functional Assessment of Cancer Therapy-Leukemia, HRQL= health-related quality of life, Ig=immunoglobulin, IWRS=interactive web response system, MRI= magnetic resonance imaging

Appendix 2. Testing Strategy for secondary endpoints

The primary endpoint of Study 312-0119, PFS, will be analyzed using the group sequential O'Brien Fleming method with 2 interim analyses and 1 final analysis. Even though 2-sided alpha level is used in this study, for simplicity, 1-sided alpha level is used in Appendix 2 as 2-sided type I error is 2 times 1-sided type I error in testing superiority of the active arm over the control arm. The overall 1-sided family-wise type I error rate for this study is set to be 0.025. Given the OF boundaries and the pre-specified gate-keeping procedure for primary and secondary endpoints, we here justify the use of 1-sided boundary of 0.015 for the testing of secondary endpoints in both the interim and final analyses following the methods in Hung et al (2007) {26737}, and Tamhane et al (2010) {30874}.

Per Hung et al {26737} the type I error rate for the secondary endpoint in the hierarchical testing strategy is:

$$\alpha_2 = \Pr(T_{11} > C_{11}, T_{21} > C_{21} \mid H_{02}) + \Pr(T_{11} \le C_{11}, T_{12} > C_{12}, T_{22} > C_{22} \mid H_{02}) \quad (1)$$

where the first subscript pertains to the endpoint (1=primary, 2=secondary) and the second subscript pertains to the analysis (1=interim, 2=final). T_{11} and C_{11} are the test statistic and critical value for the primary endpoint (PFS) at the first analysis, respectively. Similarly, T_{21} and C_{21} is the test statistic and the critical value for OS at the first analysis.

T_{12} and C_{12} are the test statistic and the critical value for PFS at the second analysis, respectively, and T_{22} and C_{22} are the test statistic and the critical value for OS at the second analysis , respectively. H_{02} is the null hypothesis for OS. This was given in a setting of 1 interim analysis and 1 final analysis, where analysis 1 refers to the interim analysis and 2 refers to the final analysis. Accordingly it can be written as:

$$\alpha_2 = \Pr(Z_{11} > z_{11}, Z_{21} > z_{21} \mid H_{02}) + \Pr(Z_{11} \le z_{11}, Z_{12} > z_{12}, Z_{22} > z_{22} \mid H_{02}) \quad (2)$$

where Z_{11} and z_{11} are the corresponding test statistics and critical values expressed in the setting of the standard normal distribution (ie, after standardization).

Extend this to the setting of Study 312-0119, where there were to be 2 interims and 1 final analyses (3 analyses in total):

$$\begin{aligned}\alpha_2 = {} & \Pr(Z_{11} > z_{11}, Z_{21} > z_{21} \mid H_{02}) + \Pr(Z_{11} \le z_{11}, Z_{12} > z_{12}, Z_{22} > z_{22} \mid H_{02}) + \\ & \Pr(Z_{11} \le z_{11}, Z_{12} \le z_{12}, Z_{13} > z_{13}, Z_{33} > z_{33} \mid H_{02})\end{aligned} \quad (3)$$

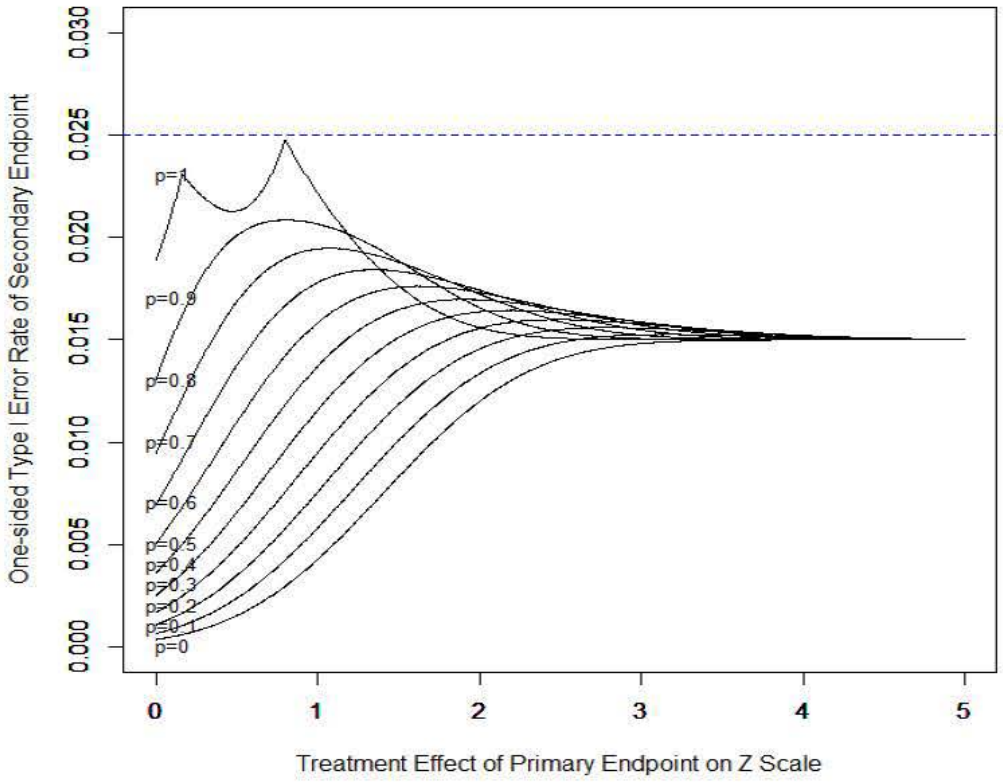
Assume $\widetilde{Z} = (Z_{11}, Z_{21}, Z_{12}, Z_{22}, Z_{13}, Z_{23})$ follows a multivariate normal distribution, it can be derived that:

$$\begin{pmatrix} Z_{11} \\ Z_{21} \\ Z_{12} \\ Z_{22} \\ Z_{13} \\ Z_{23} \end{pmatrix} \sim MVN\left(\begin{pmatrix} \mu_{11} \\ \mu_{21} \\ \mu_{12} \\ \mu_{22} \\ \mu_{13} \\ \mu_{23} \end{pmatrix}, \begin{pmatrix} 1, \rho, \sqrt{t_1/t_2}, \rho\sqrt{t_1/t_2}, \sqrt{t_1}, \rho\sqrt{t_1} \\ \rho, 1, \rho\sqrt{t_1/t_2}, \sqrt{t_1/t_2}, \rho\sqrt{t_1}, \sqrt{t_1} \\ \sqrt{t_1/t_2}, \rho\sqrt{t_1/t_2}, 1, \rho, \sqrt{t_2}, \rho\sqrt{t_2} \\ \rho\sqrt{t_1/t_2}, \sqrt{t_1/t_2}, \rho, 1, \rho\sqrt{t_2}, \sqrt{t_2} \\ \sqrt{t_1}, \rho\sqrt{t_1}, \sqrt{t_2}, \rho\sqrt{t_2}, 1, \rho \\ \rho\sqrt{t_1}, \sqrt{t_1}, \rho\sqrt{t_2}, \sqrt{t_2}, \rho, 1 \end{pmatrix} \right) \quad (4)$$

where $(\mu_{11}, \mu_{12}, \mu_{13})$ are the normalized mean treatment effect on the primary endpoint for the data up to the first interim, the second interim, and the final analysis; and $(\mu_{21}, \mu_{22}, \mu_{23})$ are the normalized mean treatment effect on the secondary endpoint for the data up to the first pre-specified interim, the second pre-specified interim, and the final analysis. $(\mu_{11}, \mu_{12}, \mu_{13})$ depend on the assumed true treatment effect on the primary endpoint, $(\mu_{21}, \mu_{22}, \mu_{23}) = (0,0,0)$ under the null hypothesis. ρ denotes the correlation of test statistics between the primary and the secondary test statistics at each analysis stage, with range from 0 to 1 by assuming a non-negative correlation between the primary and the secondary endpoints. $t_1 = 0.5$ and $t_2 = 0.75$ are the information fractions at the first and second pre-specified interim analyses in our study. The one-sided OF boundaries for primary endpoints are given, $z_{11}=z_{0.0015}$, $z_{12}=z_{0.009}$ and $z_{13}=z_{0.022}$. Hence, equation (3) can be calculated used the pmvnorm function in the R package mvtnorm based on the covariance structure specified in equation (4).

Appendix Figure 1 below shows the analytically calculated type I error rate for the secondary endpoint when $\alpha_2 \leq 0.025$. It demonstrates that the use of 1-sided boundary of 0.015 for the testing of secondary endpoints in both the interims and final analyses controls the Type I error rate regardless of the correlation between the primary and the secondary test statistics and the magnitude of treatment effect of primary endpoint.

Appendix Figure 1. Type I Error Rate of Secondary Endpoint in a GS design with OF boundaries for Primary Endpoints and One-sided Boundary of Alpha Level 0.015 for the Secondary Endpoints at Two Interim Analyses and One Final Analysis



Appendix 3. Table of Contents for Statistical Tables, Figures, and Listings

Table Number	Title	Analysis Set	Interim
1.1.1	Subject Study Disposition	ITT	√
1.1.2	Subject Study Disposition	PP	√
1.1.3	Subject Study Disposition by 12-weeks Interval	ITT	
1.1.4	Subject Study Treatment Disposition	ITT	√
1.1.5	Subject Study Treatment Disposition	PP	√
1.2	Summary of Enrollment by Site	ITT	√
1.3	Analysis Set	ITT	√
1.4	Important Protocol Deviations	ITT	√
1.5	Subject Distribution by Stratification Factors	ITT	√
1.6	Subject Demographics and Baseline Characteristics	ITT	√
1.6.1	Subject Demographics and Baseline Characteristics - del17p/TP53 Mutation (Either)	ITT	√
1.6.2	Subject Demographics and Baseline Characteristics - del17p/TP53 Mutation (Neither)	ITT	√
1.6.3	Subject Demographics and Baseline Characteristics – IgHV Mutated	ITT	√
1.6.4	Subject Demographics and Baseline Characteristics – IgHV Unmutated	ITT	√
1.7	CLL Disease History	ITT	√
1.8	Prior Therapy	ITT	√
1.9	Prior Radiation Therapy	ITT	√
1.10	Cumulative Illness Rating Scale (CIRS) Scores	ITT	√
1.10.1	Estimated Creatinine Clearance (eCcr) at Baseline	ITT	√
1.11	Study Drug (IDELA) Exposure	Safety	√
1.12	Ofatumumab Exposure	Safety	√
1.13	Summary of Dose Modification of IDELA	Safety	√
1.14	Duration of Study	ITT	√
1.15	Time to Discontinuation from Study	ITT	.
2.1.1	Progression-free Survival by IRC Assessment	ITT	√
2.1.1.1	Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.1.1.2	Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√

Table Number	Title	Analysis Set	Interim
2.1.1.3	Progression-free Survival by IRC Assessment – IgHV Mutated	ITT	√
2.1.1.4	Progression-free Survival by IRC Assessment – IgHV Unmutated	ITT	√
2.1.1.5	Progression-free Survival by IRC Assessment - 17p deletion	ITT	√
2.1.1.6	Progression-free Survival by IRC Assessment – No 17p deletion	ITT	√
2.1.1.7	Progression-free Survival by IRC Assessment – Refractory Status	ITT	√
2.1.1.8	Progression-free Survival by IRC Assessment – Relapsed Status	ITT	√
2.1.1.9	Progression-free Survival by IRC Assessment - Male	ITT	√
2.1.1.10	Progression-free Survival by IRC Assessment - Female	ITT	√
2.1.1.11	Progression-free Survival by IRC Assessment – Age < 65 (years)	ITT	√
2.1.1.12	Progression-free Survival by IRC Assessment – Age >= 65 (years)	ITT	√
2.1.1.13	Progression-free Survival by IRC Assessment - Race White	ITT	√
2.1.1.14	Progression-free Survival by IRC Assessment - Race Non-White	ITT	√
2.1.1.15	Cox Regression for Progression-free Survival by IRC Assessment	ITT	
2.1.2	Progression-free Survival by IRC Assessment	PP	√
2.1.2.1	Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Either)	PP	√
2.1.2.2	Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Neither)	PP	√
2.1.2.3	Progression-free Survival by IRC Assessment - IgHV Mutated	PP	√
2.1.2.4	Progression-free Survival by IRC Assessment - IgHV Unmutated	PP	√
2.1.2.5	Progression-free Survival by IRC Assessment - Relapsed Disease Status	PP	√
2.1.2.6	Progression-free Survival by IRC Assessment - Refractory Disease Status	PP	√
2.1.2.7	Progression-free Survival Sensitivity Analysis by IRC Assessment	ITT	
2.1.3.1	Progression-free Survival Using the Unstratified Log-rank Test (Sensitivity Analysis) by IRC Assessment	ITT	√

Table Number	Title	Analysis Set	Interim
2.1.3.2	Progression-free Survival (Worst Case Sensitivity Analysis) by IRC Assessment	ITT	√
2.1.4	Progression-free Survival by IRC Assessment with Inverse Probability Censoring Weighted	ITT	
2.1.5	Progression-free Survival by Investigator Assessment	ITT	√
2.1.6	Disease Progression Criteria	ITT	
2.2.1	Overall Response Rate (ORR) by IRC Assessment	ITT	√
2.2.1.1	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.2.1.2	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.2.1.3	Overall Response Rate (ORR) by IRC Assessment - IgHV Mutated	ITT	√
2.2.1.4	Overall Response Rate (ORR) by IRC Assessment - IgHV Unmutated	ITT	√
2.2.1.5	Overall Response Rate (ORR) by IRC Assessment - 17p deletion	ITT	√
2.2.1.6	Overall Response Rate (ORR) by IRC Assessment – No 17p deletion	ITT	√
2.2.1.7	Overall Response Rate (ORR) by IRC Assessment - Refractory Disease Status	ITT	√
2.2.1.8	Overall Response Rate (ORR) by IRC Assessment - Relapsed Disease Status	ITT	√
2.2.1.9	Overall Response Rate (ORR) by IRC Assessment - Male	ITT	√
2.2.1.10	Overall Response Rate (ORR) by IRC Assessment - Female	ITT	√
2.2.1.11	Overall Response Rate (ORR) by IRC Assessment – Age < 65 (years)	ITT	√
2.2.1.12	Overall Response Rate (ORR) by IRC Assessment – Age >= 65 (years)	ITT	√
2.2.1.13	Overall Response Rate (ORR) by IRC Assessment - Race White	ITT	√
2.2.1.14	Overall Response Rate (ORR) by IRC Assessment - Race Non-White	ITT	√
2.2.1.15	Logistic Regression for Overall Response Rate (ORR) by IRC Assessment	ITT	
2.2.4	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment	ITT	√
2.2.4.1	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√

Table Number	Title	Analysis Set	Interim
2.2.4.2	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.2.4.3	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - IgHV Mutated	ITT	√
2.2.4.4	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - IgHV Unmutated	ITT	√
2.2.4.5	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - 17p deletion	ITT	√
2.2.4.6	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - No 17p deletion	ITT	√
2.2.4.7	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Refractory Disease Status	ITT	√
2.2.4.8	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Relapsed Disease Status	ITT	√
2.2.4.9	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Male	ITT	√
2.2.4.10	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Female	ITT	√
2.2.4.11	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Age < 65 (years)	ITT	√
2.2.4.12	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Age >= 65 (years)	ITT	√
2.2.4.13	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Race White	ITT	√
2.2.4.14	Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment - Race Non-White	ITT	√
2.2.4.15	Logistic Regression for Overall Response Rate (ORR) Sensitivity Analysis by IRC Assessment	ITT	
2.2.2	Overall Response Rate (ORR) by IRC Assessment	PP	√
2.2.2.1	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Either)	PP	√
2.2.2.2	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Neither)	PP	√
2.2.2.3	Overall Response Rate (ORR) by IRC Assessment - IgHV Mutated	PP	√
2.2.2.4	Overall Response Rate (ORR) by IRC Assessment - IgHV Unmutated	PP	√
2.2.2.5	Overall Response Rate (ORR) by IRC Assessment - 17p deletion	PP	√

Table Number	Title	Analysis Set	Interim
2.2.2.6	Overall Response Rate (ORR) by IRC Assessment - No 17p deletion	PP	√
2.2.2.7	Overall Response Rate (ORR) by IRC Assessment - Refractory Disease Status	PP	√
2.2.2.8	Overall Response Rate (ORR) by IRC Assessment - Relapsed Disease Status	PP	√
2.2.3	Overall Response Rate (ORR) by IRC Assessment	ITT with at least One Post Baseline Assessment	√
2.2.3.1	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT with at least One Post Baseline Assessment	√
2.2.3.2	Overall Response Rate (ORR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT with at least One Post Baseline Assessment	√
2.2.3.3	Overall Response Rate (ORR) by IRC Assessment - IgHV Mutated	ITT with at least One Post Baseline Assessment	√
2.2.3.4	Overall Response Rate (ORR) by IRC Assessment - IgHV Unmutated	ITT with at least One Post Baseline Assessment	√
2.2.3.5	Overall Response Rate (ORR) by IRC Assessment - 17p deletion	ITT with at least One Post Baseline Assessment	√
2.2.3.6	Overall Response Rate (ORR) by IRC Assessment - No 17p deletion	ITT with at least One Post Baseline Assessment	√
2.2.3.7	Overall Response Rate (ORR) by IRC Assessment - Relapsed Disease Status	ITT with at least One Post Baseline Assessment	√
2.2.3.8	Overall Response Rate (ORR) by IRC Assessment - Refractory Disease Status	ITT with at least One Post Baseline Assessment	√
2.2.3.9	Overall Response Rate (ORR) by IRC Assessment - Male	ITT with at least One Post Baseline Assessment	√
2.2.3.10	Overall Response Rate (ORR) by IRC Assessment - Female	ITT with at least One Post Baseline Assessment	√
2.2.3.11	Overall Response Rate (ORR) by IRC Assessment – Age < 65 (years)	ITT with at least One Post Baseline Assessment	√

Table Number	Title	Analysis Set	Interim
2.2.3.12	Overall Response Rate (ORR) by IRC Assessment – Age >= 65 (years)	ITT with at least One Post Baseline Assessment	√
2.2.3.13	Overall Response Rate (ORR) by IRC Assessment - Race White	ITT with at least One Post Baseline Assessment	√
2.2.3.14	Overall Response Rate (ORR) by IRC Assessment - Race Non-White	ITT with at least One Post Baseline Assessment	√
2.2.5	Overall Response Rate (ORR) by Investigator Assessment	ITT	√
2.2.5.1	Overall Response Rate (ORR) by Investigator Assessment (Without 8 Weeks Confirmation)	ITT	√
2.2.6	Agreement in Overall Response Rate (ORR) between IRC and Investigator Assessment	ITT	√
2.2.6.1	Agreement in Overall Response Rate (ORR) between IRC and Investigator Assessment (Without 8 Weeks Confirmation)	ITT	√
2.3.1	Complete Response Rate (CR) by IRC Assessment	ITT	
2.3.1.1	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	
2.3.1.2	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	
2.3.1.3	Complete Response Rate (CR) by IRC Assessment - IgHV Mutated	ITT	
2.3.1.4	Complete Response Rate (CR) by IRC Assessment - IgHV Unmutated	ITT	
2.3.1.5	Complete Response Rate (CR) by IRC Assessment - 17p deletion	ITT	
2.3.1.6	Complete Response Rate (CR) by IRC Assessment - No 17p deletion	ITT	
2.3.1.7	Complete Response Rate (CR) by IRC Assessment - Refractory Disease Status	ITT	
2.3.1.8	Complete Response Rate (CR) by IRC Assessment - Relapsed Disease Status	ITT	
2.3.1.9	Complete Response Rate (CR) by IRC Assessment - Male	ITT	
2.3.1.10	Complete Response Rate (CR) by IRC Assessment - Female	ITT	
2.3.1.11	Complete Response Rate (CR) by IRC Assessment – Age < 65 (years)	ITT	
2.3.1.12	Complete Response Rate (CR) by IRC Assessment – Age >= 65 (years)	ITT	

Table Number	Title	Analysis Set	Interim
2.3.1.13	Complete Response Rate (CR) by IRC Assessment - Race White	ITT	
2.3.1.14	Complete Response Rate (CR) by IRC Assessment - Race Non-White	ITT	
2.3.1.15	Logistic Regression for Complete Response Rate (CR) by IRC Assessment	ITT	
2.3.2	Complete Response Rate (CR) by IRC Assessment	PP	
2.3.2.1	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Either)	PP	
2.3.2.2	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Neither)	PP	
2.3.2.3	Complete Response Rate (CR) by IRC Assessment - IgHV Mutated	PP	
2.3.2.4	Complete Response Rate (CR) by IRC Assessment - IgHV Unmutated	PP	
2.3.2.5	Complete Response Rate (CR) by IRC Assessment - 17p deletion	PP	
2.3.2.6	Complete Response Rate (CR) by IRC Assessment - No 17p deletion	PP	
2.3.2.7	Complete Response Rate (CR) by IRC Assessment - Refractory Disease Status	PP	
2.3.2.8	Complete Response Rate (CR) by IRC Assessment - Relapsed Disease Status	PP	
2.3.3	Complete Response Rate (CR) by IRC Assessment	ITT with at least One Post Baseline Assessment	
2.3.3.1	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT with at least One Post Baseline Assessment	
2.3.3.2	Complete Response Rate (CR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT with at least One Post Baseline Assessment	
2.3.3.3	Complete Response Rate (CR) by IRC Assessment - IgHV Mutated	ITT with at least One Post Baseline Assessment	
2.3.3.4	Complete Response Rate (CR) by IRC Assessment - IgHV Unmutated	ITT with at least One Post Baseline Assessment	
2.3.3.5	Complete Response Rate (CR) by IRC Assessment - 17p deletion	ITT with at least One Post Baseline Assessment	

Table Number	Title	Analysis Set	Interim
2.3.3.6	Complete Response Rate (CR) by IRC Assessment – No 17p deletion	ITT with at least One Post Baseline Assessment	
2.3.3.7	Complete Response Rate (ORR) by IRC Assessment - Refractory Disease Status	ITT with at least One Post Baseline Assessment	
2.3.3.8	Complete Response Rate (ORR) by IRC Assessment - Relapsed Disease Status	ITT with at least One Post Baseline Assessment	
2.3.3.9	Complete Response Rate (CR) by IRC Assessment - Male	ITT with at least One Post Baseline Assessment	
2.3.3.10	Complete Response Rate (CR by IRC Assessment - Female	ITT with at least One Post Baseline Assessment	
2.3.3.11	Complete Response Rate (CR) by IRC Assessment – Age < 65 (years)	ITT with at least One Post Baseline Assessment	
2.3.3.12	Complete Response Rate (CR) by IRC Assessment – Age >= 65 (years)	ITT with at least One Post Baseline Assessment	
2.3.3.13	Complete Response Rate (CR) by IRC Assessment - Race White	ITT with at least One Post Baseline Assessment	
2.3.3.14	Complete Response Rate (CR) by IRC Assessment - Race Non-White	ITT with at least One Post Baseline Assessment	
2.3.4	Complete Response Rate (CR) by Investigator Assessment	ITT	
2.3.5	Agreement in Complete Response Rate (CR) between IRC and Investigator Assessment	ITT	
2.4.1	Lymph Node Response (LNR) Rate by IRC Assessment	ITT	√
2.4.1.1	Lymph Node Response (LNR) Rate by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.4.1.2	Lymph Node Response (LNR) Rate by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.4.1.3	Lymph Node Response (LNR) Rate by IRC Assessment - IgHV Mutated	ITT	√
2.4.1.4	Lymph Node Response (LNR) Rate by IRC Assessment - IgHV Unmutated	ITT	√
2.4.1.5	Lymph Node Response (LNR) Rate by IRC Assessment - 17p deletion	ITT	√

Table Number	Title	Analysis Set	Interim
2.4.1.6	Lymph Node Response (LNR) Rate by IRC Assessment - No 17p deletion	ITT	√
2.4.1.7	Lymph Node Response (LNR) Rate by IRC Assessment - Refractory Disease Status	ITT	√
2.4.1.8	Lymph Node Response (LNR) Rate by IRC Assessment - Relapsed Disease Status	ITT	√
2.4.1.9	Lymph Node Response (LNR) Rate by IRC Assessment - Male	ITT	√
2.4.1.10	Lymph Node Response (LNR) Rate by IRC Assessment - Female	ITT	√
2.4.1.11	Lymph Node Response (LNR) Rate by IRC Assessment - Age < 65 (years)	ITT	√
2.4.1.12	Lymph Node Response (LNR) Rate by IRC Assessment - Age >= 65 (years)	ITT	√
2.4.1.13	Lymph Node Response (LNR) Rate by IRC Assessment - Race White	ITT	√
2.4.1.14	Lymph Node Response (LNR) Rate by IRC Assessment - Race Non-White	ITT	√
2.4.1.15	Logistic Regression for Lymph Node Response (LNR) Rate by IRC Assessment	ITT	
2.4.2	Lymph Node Response (LNR) Rate by IRC Assessment	PP	√
2.4.2.1	Lymph Node Response (LNR) Rate by IRC Assessment - del17p/TP53 Mutation (Either)	PP	√
2.4.2.2	Lymph Node Response (LNR) Rate by IRC Assessment - del17p/TP53 Mutation (Neither)	PP	√
2.4.2.3	Lymph Node Response (LNR) Rate by IRC Assessment - IgHV Mutated	PP	√
2.4.2.4	Lymph Node Response (LNR) Rate by IRC Assessment - IgHV Unmutated	PP	√
2.4.2.5	Lymph Node Response (LNR) Rate by IRC Assessment - 17p deletion	PP	√
2.4.2.6	Lymph Node Response (LNR) Rate by IRC Assessment - No 17p deletion	PP	√
2.4.2.7	Lymph Node Response (LNR) Rate by IRC Assessment - Refractory Disease Status	PP	√
2.4.2.8	Lymph Node Response (LNR) Rate by IRC Assessment - Relapsed Disease Status	PP	√
2.5.1	Overall Survival (OS)	ITT	√
2.5.1.1	Overall Survival (OS) - del17p/TP53 Mutation (Either)	ITT	√

Table Number	Title	Analysis Set	Interim
2.5.1.2	Overall Survival (OS) - del17p/TP53 Mutation (Neither)	ITT	√
2.5.1.3	Overall Survival (OS) - IgHV Mutated	ITT	√
2.5.1.4	Overall Survival (OS) - IgHV Unmutated	ITT	√
2.5.1.5	Overall Survival (OS) - 17p deletion	ITT	√
2.5.1.6	Overall Survival (OS) - No 17p deletion	ITT	√
2.5.1.7	Overall Survival (OS) - Refractory Disease Status	ITT	√
2.5.1.8	Overall Survival (OS) - Relapsed Disease Status	ITT	√
2.5.1.9	Overall Survival (OS) - Male	ITT	√
2.5.1.10	Overall Survival (OS) - Female	ITT	√
2.5.1.11	Overall Survival (OS) - Age < 65 (years)	ITT	√
2.5.1.12	Overall Survival (OS) - Age >= 65 (years)	ITT	√
2.5.1.13	Overall Survival (OS) - Race White	ITT	√
2.5.1.14	Overall Survival (OS) - Race Non-White	ITT	√
2.5.1.15	Cox Regression for Overall Survival (OS)	ITT	
2.6.1	Time to Response (TTR) by IRC Assessment	ITT	√
2.6.1.1	Time to Response (TTR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.6.1.2	Time to Response (TTR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.6.1.3	Time to Response (TTR) by IRC Assessment - IgHV Mutated	ITT	√
2.6.1.4	Time to Response (TTR) by IRC Assessment - IgHV Unmutated	ITT	√
2.6.1.5	Time to Response (TTR) by IRC Assessment - 17p deletion	ITT	√
2.6.1.6	Time to Response (TTR) by IRC Assessment - No 17p deletion	ITT	√
2.6.1.7	Time to Response (TTR) by IRC Assessment - Refractory Disease Status	ITT	√
2.6.1.8	Time to Response (TTR) by IRC Assessment - Relapsed Disease Status	ITT	√
2.6.1.9	Time to Response (TTR) by IRC Assessment - Male	ITT	√
2.6.1.10	Time to Response (TTR) by IRC Assessment - Female	ITT	√
2.6.1.11	Time to Response (TTR) by IRC Assessment – Age < 65 (years)	ITT	√

Table Number	Title	Analysis Set	Interim
2.6.1.12	Time to Response (TTR) by IRC Assessment – Age >= 65 (years)	ITT	√
2.6.1.13	Time to Response (TTR) by IRC Assessment - Race White	ITT	√
2.6.1.14	Time to Response (TTR) by IRC Assessment - Race Non-White	ITT	√
2.6.2	Time to Response (TTR) Sensitivity Analysis by IRC Assessment	ITT	√
2.6.2.1	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.6.2.2	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.6.2.3	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - IgHV Mutated	ITT	√
2.6.2.4	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - IgHV Unmutated	ITT	√
2.6.2.5	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - 17p deletion	ITT	√
2.6.2.6	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - No 17p Deletion	ITT	√
2.6.2.7	Time to Response (TTR) Sensitivity Analysis Sensitivity Analysis by IRC Assessment - Refractory Disease Status	ITT	√
2.6.2.8	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Relapsed Disease Status	ITT	√
2.6.2.9	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Male	ITT	√
2.6.2.10	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Female	ITT	√
2.6.2.11	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Age < 65 (years)	ITT	√
2.6.2.12	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Age >= 65 (years)	ITT	√
2.6.2.13	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Race White	ITT	√
2.6.2.14	Time to Response (TTR) Sensitivity Analysis by IRC Assessment - Race Non-White	ITT	√
2.6.3	Time to Response (TTR) by IRC Assessment	PP	√
2.6.4.1	Time to Response (TTR) by Investigator Assessment (Without 8 Weeks Confirmation)	ITT	√
2.7.1	Duration of Response (DOR) by IRC Assessment	ITT	√

Table Number	Title	Analysis Set	Interim
2.7.1.1	Duration of Response (DOR) by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.7.1.2	Duration of Response (DOR) by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.7.1.3	Duration of Response (DOR) by IRC Assessment - IgHV Mutated	ITT	√
2.7.1.4	Duration of Response (DOR) by IRC Assessment - IgHV Unmutated	ITT	√
2.7.1.5	Duration of Response (DOR) by IRC Assessment - 17p deletion	ITT	√
2.7.1.6	Duration of Response (DOR) by IRC Assessment - No 17p deletion	ITT	√
2.7.1.7	Duration of Response (DOR) by IRC Assessment - Refractory Disease Status	ITT	√
2.7.1.8	Duration of Response (DOR) by IRC Assessment - Relapsed Disease Status	ITT	√
2.7.1.9	Duration of Response (DOR) by IRC Assessment - Male	ITT	√
2.7.1.10	Duration of Response (DOR) by IRC Assessment - Female	ITT	√
2.7.1.11	Duration of Response (DOR) by IRC Assessment – Age < 65 (years)	ITT	√
2.7.1.12	Duration of Response (DOR) by IRC Assessment – Age >= 65 (years)	ITT	√
2.7.1.13	Duration of Response (DOR) by IRC Assessment - Race White	ITT	√
2.7.1.14	Duration of Response (DOR) by IRC Assessment - Race Non-White	ITT	√
2.7.2	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment	ITT	√
2.7.2.1	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.7.2.2	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.7.2.3	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - IgHV Mutated	ITT	√
2.7.2.4	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - IgHV Unmutated	ITT	√
2.7.2.5	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - 17p deletion	ITT	√
2.7.2.6	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - No 17p deletion	ITT	√

Table Number	Title	Analysis Set	Interim
2.7.2.7	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Refractory Disease Status	ITT	√
2.7.2.8	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Relapsed Disease Status	ITT	√
2.7.2.9	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Male	ITT	√
2.7.2.10	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Female	ITT	√
2.7.2.11	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Age < 65 (years)	ITT	√
2.7.2.12	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Age >= 65 (years)	ITT	√
2.7.2.13	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Race White	ITT	√
2.7.2.14	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment - Race Non-White	ITT	√
2.7.3	Duration of Response (DOR) Sensitivity Analysis by IRC Assessment	PP	√
2.7.4.1	Duration of Response (DOR) Sensitivity Analysis by Investigator Assessment (Without 8 Weeks Confirmation)	ITT	√
2.8	Best Percent Change in SPD - IRC assessment	ITT	√
2.8.1	Best Percent Change in SPD by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
2.8.2	Best Percent Change in SPD by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
2.8.3	Best Percent Change in SPD by IRC Assessment - IgHV Mutated	ITT	√
2.8.4	Best Percent Change in SPD by IRC Assessment - IgHV Unmutated	ITT	√
2.8.5	Best Percent Change in SPD by IRC Assessment - 17p deletion	ITT	√
2.8.6	Best Percent Change in SPD by IRC Assessment - No 17p deletion	ITT	√
2.8.7	Best Percent Change in SPD by IRC Assessment - Refractory Disease Status	ITT	√
2.8.8	Best Percent Change in SPD by IRC Assessment - Relapsed Disease Status	ITT	√
2.9.1	Baseline Abnormality Status for Efficacy Response Assessment	ITT	√
2.9.2	Splenomegaly Response Rate - IRC Assessment	ITT	√

Table Number	Title	Analysis Set	Interim
2.9.3	Hepatomegaly Response Rate - IRC Assessment	ITT	√
2.9.4	ALC Response Rate	ITT	√
2.9.5	Platelet Response Rate	ITT	√
2.9.6	Hemoglobin Response Rate	ITT	√
2.9.7	Neutrophil (ANC) Response Rate	ITT	√
2.10.1	CT/MRI Assessment by Investigator	ITT	√
2.10.2	CLL Assessment by Physical Examination	ITT	√
2.11.1.1	Functional Assessment of Cancer Therapy: Leukemia (FACT-Leu) - Actual and Change from Baseline	ITT	√
2.11.1.2	Mixed Model for Functional Assessment of Cancer Therapy: Leukemia (FACT-Leu)	ITT	
2.11.1.3	Functional Assessment of Cancer Therapy: Leukemia (FACT-Leu) - Compliance	ITT	√
2.11.2.1	Karnofsky Performance Status - Observed and Change from Baseline	ITT	√
2.11.3.1	Summary of EuroQoL Five Dimension Descriptive System (EQ-5D) by Dimension	ITT	√
2.11.3.2	Summary of EuroQol Visual Analogue Score (VAS) - Actual Values and Change from Baseline	ITT	√
2.11.3.3	Summary of EuroQol Five Dimension Questionnaire Utility Index - Actual Values and Change from Baseline	ITT	
2.11.3.4	Mixed Model for EuroQoL Five Dimension Questionnaire (EQ-5D)	ITT	
2.11.3.5	Mixed Model for EuroQoL Five Dimension Questionnaire Utility Index (EQ-5D)	ITT	
2.11.3.6	EuroQEuroQoL Five Dimension Questionnaire (EQ-5D) - Compliance	ITT	√
3.1.1	Overall Summary of Adverse Events	Safety	√
3.1.1.1	Overall Summary of Adverse Events - Male	Safety	√
3.1.1.2	Overall Summary of Adverse Events - Female	Safety	√
3.1.1.3	Overall Summary of Adverse Events - Age < 65 (years)	Safety	√
3.1.1.4	Overall Summary of Adverse Events - Age >= 65 (years)	Safety	√
3.1.1.5	Overall Summary of Adverse Events - Race White	Safety	√
3.1.1.6	Overall Summary of Adverse Events - Race Non-White	Safety	√
3.1.2	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.2.1	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.2.2	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.2.3	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.2.4	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age >=65 (years)	Safety	√
3.1.2.5	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.2.6	Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.3	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade	Safety	√
3.1.3.1	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Male	Safety	√
3.1.3.2	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Female	Safety	√
3.1.3.3	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Age < 65 (years)	Safety	√
3.1.3.4	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Age >=65 (years)	Safety	√
3.1.3.5	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Race White	Safety	√
3.1.3.6	Treatment-Emergent Adverse Events by MedDRA SOC, HLT, PT and CTCAE Grade - Race Non-White	Safety	√
3.1.4	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade	Safety	√
3.1.4.1	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Male	Safety	√
3.1.4.2	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Female	Safety	√
3.1.4.3	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Age < 65 (years)	Safety	√
3.1.4.4	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade – Age >= 65 (years)	Safety	√
3.1.4.5	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Race White	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.4.6	Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Race Non-White	Safety	√
3.1.5	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade	Safety	√
3.1.5.1	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade - Male	Safety	√
3.1.5.2	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade - Female	Safety	√
3.1.5.3	Treatment-Emergent Adverse Events Related to Ofatumamub by MedDRA SOC, HLT, PT, and CTCAE Grade - Age < 65 (years)	Safety	√
3.1.5.4	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade - Age >= 65 (years)	Safety	√
3.1.5.5	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade - Race White	Safety	√
3.1.5.6	Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT, PT, and CTCAE Grade - Race Non-White	Safety	√
3.1.6	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT	Safety	√
3.1.6.1	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.6.2	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.6.3	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.6.4	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age >=65 (years)	Safety	√
3.1.6.5	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.6.6	Grade >= 3 Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.7	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT	Safety	√
3.1.7.1	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Male	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.7.2	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.7.3	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.7.4	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Age >= 65 (years)	Safety	√
3.1.7.5	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.7.6	Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.8	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT	Safety	√
3.1.8.1	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.8.2	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.8.3	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT – Age < 65 (years)	Safety	√
3.1.8.4	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT – Age >=65 (years)	Safety	√
3.1.8.5	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.8.6	Grade >= 3 Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.9	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT	Safety	√
3.1.9.1	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.9.2	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.9.3	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.9.4	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Age >= 65 (years)	Safety	√
3.1.9.5	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.9.6	Serious Treatment-Emergent Adverse Events by MedDRA SOC, HLT and PT - Race Non-White	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.10	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT	Safety	√
3.1.10.1	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.10.2	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.10.3	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.10.4	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Age >= 65 (years)	Safety	√
3.1.10.5	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.10.6	Serious Treatment-Emergent Adverse Events Related to IDELA by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.11	Serious Treatment-Emergent Adverse Events Related to Ofatumamub by MedDRA SOC, HLT and PT	Safety	√
3.1.11.1	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.11.2	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.11.3	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT – Age < 65 (years)	Safety	√
3.1.11.4	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT – Age >= 65 (years)	Safety	√
3.1.11.5	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.11.6	Serious Treatment-Emergent Adverse Events Related to Ofatumumab by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.12	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade	Safety	√
3.1.12.1	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Male	Safety	√
3.1.12.2	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Female	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.12.3	TEAEs Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade – Age < 65 (years)	Safety	√
3.1.12.4	TEAEs Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade – Age >= 65 (years)	Safety	√
3.1.12.5	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Race White	Safety	√
3.1.12.6	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA SOC, HLT, PT and CTCAE Grade - Race Non-White	Safety	√
3.1.13	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT	Safety	√
3.1.13.1	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.13.2	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.13.3	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT – Age < 65 (years)	Safety	√
3.1.13.4	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT – Age >= 65 (years)	Safety	√
3.1.13.5	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.13.6	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.28	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT	Safety	√
3.1.28.1	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.28.2	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.28.3	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT – Age < 65 (years)	Safety	√
3.1.28.4	Treatment-Emergent Adverse Events Leading toOfatumumab Delay by MedDRA SOC, HLT and PT – Age >= 65 (years)	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.28.5	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.28.6	Treatment-Emergent Adverse Events Leading to Ofatumumab Delay by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.29	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT	Safety	√
3.1.29.1	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.29.2	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.29.3	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.29.4	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Age >= 65 (years)	Safety	√
3.1.29.5	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.29.6	Treatment-Emergent Adverse Events Leading to Ofatumumab Discontinuation by MedDRA SOC, HLT and PT - Race Non-White	Safety	√
3.1.14	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT	Safety	√
3.1.14.1	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Male	Safety	√
3.1.14.2	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Female	Safety	√
3.1.14.3	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Age < 65 (years)	Safety	√
3.1.14.4	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Age >= 65 (years)	Safety	√
3.1.14.5	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Race White	Safety	√
3.1.14.6	Treatment-Emergent Adverse Events Leading to Death by MedDRA SOC, HLT and PT - Race Non-White	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.15	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade	Safety	√
3.1.15.1	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Male	Safety	√
3.1.15.2	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Female	Safety	√
3.1.15.3	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Age < 65 (years)	Safety	√
3.1.15.4	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Age >= 65 (years)	Safety	√
3.1.15.5	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Race White	Safety	√
3.1.15.6	Treatment-Emergent Adverse Events by MedDRA PT and CTCAE Grade - Race Non-White	Safety	√
3.1.16	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT	Safety	√
3.1.16.1	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Male	Safety	√
3.1.16.2	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Female	Safety	√
3.1.16.3	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Age < 65 (years)	Safety	√
3.1.16.4	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Age >= 65 (years)	Safety	√
3.1.16.5	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Race White	Safety	√
3.1.16.6	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT - Race Non-White	Safety	√
3.1.16.7	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (0 to 12 Weeks)	Safety	
3.1.16.8	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (12 to 24 Weeks)	Safety at 12 Weeks	
3.1.16.9	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (24 to 36 Weeks)	Safety at 24 Weeks	
3.1.16.10	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (36 to 48 Weeks)	Safety at 36	
3.1.16.11	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (>= 48 Weeks)	Safety at 48 Weeks	
3.1.16.12	All Grades and Grade >= 3 Treatment-Emergent Adverse Events by MedDRA PT (0 to 6 month)	Safety	

Table Number	Title	Analysis Set	Interim
3.1.17	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT	Safety	√
3.1.17.1	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT - Male	Safety	√
3.1.17.2	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT - Female	Safety	√
3.1.17.3	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT – Age < 65 (years)	Safety	√
3.1.17.4	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT – Age >=65 (years)	Safety	√
3.1.17.5	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT - Race White	Safety	√
3.1.17.6	All Grades and Grade >= 3 Treatment-Emergent Adverse Events Related to IDELA by MedDRA PT - Race Non-White	Safety	√
3.1.18	Serious Treatment-Emergent Adverse Events by MedDRA PT	Safety	√
3.1.18.1	Serious Treatment-Emergent Adverse Events by MedDRA PT - Male	Safety	√
3.1.18.2	Serious Treatment-Emergent Adverse Events by MedDRA PT - Female	Safety	√
3.1.18.3	Serious Treatment-Emergent Adverse Events by MedDRA PT - Age < 65 (years)	Safety	√
3.1.18.4	Serious Treatment-Emergent Adverse Events by MedDRA PT - Age >= 65 (years)	Safety	√
3.1.18.5	Serious Treatment-Emergent Adverse Events by MedDRA PT - Race White	Safety	√
3.1.18.6	Serious Treatment-Emergent Adverse Events by MedDRA PT - Race Non-White	Safety	√
3.1.19	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade	Safety	√
3.1.19.1	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Male	Safety	√
3.1.19.2	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Female	Safety	√
3.1.19.3	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Age < 65 (years)	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.19.4	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Age >= 65 (years)	Safety	√
3.1.19.5	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Race White	Safety	√
3.1.19.6	Treatment-Emergent Adverse Events Leading to Reduction/ Interruption of IDELA by MedDRA PT and CTCAE grade - Race Non-White	Safety	√
3.1.19.7	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade	Safety	
3.1.19.8	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade - Male	Safety	
3.1.19.9	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade - Female	Safety	
3.1.19.10	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade – Age <65 (years)	Safety	
3.1.19.11	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade – Age >=65 (years)	Safety	
3.1.19.12	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade - Race White	Safety	
3.1.19.13	Treatment-Emergent Adverse Events Leading to Interruption of IDELA by MedDRA PT and CTCAE grade - Race Non-White	Safety	
3.1.19.14	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade	Safety	
3.1.19.15	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade - Male	Safety	
3.1.19.16	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade - Female	Safety	
3.1.19.17	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade – Age <65 (years)	Safety	
3.1.19.18	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade – Age >=65 (years)	Safety	
3.1.19.19	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade - Race White	Safety	

Table Number	Title	Analysis Set	Interim
3.1.19.20	Treatment-Emergent Adverse Events Leading to Reduction of IDELA by MedDRA PT and CTCAE grade - Race Non-White	Safety	
3.1.20	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT	Safety	√
3.1.20.1	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Male	Safety	√
3.1.20.2	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Female	Safety	√
3.1.20.3	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Age < 65 (years)	Safety	√
3.1.20.4	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Age >= 65 (years)	Safety	√
3.1.20.5	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Race White	Safety	√
3.1.20.6	Treatment-Emergent Adverse Events Leading to IDELA Discontinuation by MedDRA PT - Race Non-White	Safety	√
3.1.21	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT	Safety	√
3.1.21.1	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Male	Safety	√
3.1.21.2	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Female	Safety	√
3.1.21.3	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Age < 65 (years)	Safety	√
3.1.21.4	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Age >= 65 (years)	Safety	√
3.1.21.5	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Race White	Safety	√
3.1.21.6	Treatment-Emergent Adverse Events Leading to Death by MedDRA PT - Race Non-White	Safety	√
3.1.22.1	Treatment-Emergent Adverse Events with >=2% Difference Between Two Groups by MedDRA PT	Safety	
3.1.22.2	Grade >= 3 Treatment-Emergent Adverse Events with >=2% Difference Between Two Groups by MedDRA PT	Safety	
3.1.22.3	Relative Risk of Treatment-Emergent Adverse Events by MedDRA PT	Safety	√
3.1.22.4	Exposure-Adjusted Incidence Rate of Treatment-Emergent Adverse Events	Safety	√

Table Number	Title	Analysis Set	Interim
3.1.23.1	Treatment-Emergent Adverse Events of Interest by CTCAE Grade	Safety	√
3.1.23.2	Treatment-Emergent Adverse Events of Interest Leading to Reduction/ Interruption of IDELA by CTCAE Grade	Safety	√
3.1.23.3	Treatment-Emergent Adverse Events of Interest Leading to Reduction of IDELA by CTCAE Grade	Safety	√
3.1.23.4	Treatment-Emergent Adverse Events of Interest Leading to Interruption of IDELA by CTCAE Grade	Safety	
3.1.23.5	Treatment-Emergent Adverse Events of Interest Leading to IDELA Discontinuation	Safety	
3.1.23.6	Incidence of Treatment-Emergent Adverse Events of Interest by 12-weeks Intevals	Safety	
3.1.23.7	Prevalence of Treatment-Emergent Adverse Events of Interest by 12-weeks Intevals	Safety	
3.1.23.8	Exposure-Adjusted Incidence Rate of Treatment-Emergent Adverse Events of Interest	Safety	
3.1.23.9	Time to First Onset and Resolution of Treatment-Emergent Adverse Events of Interest	Safety	
3.1.23.10	Summary of Treatment-Emergent Adverse Events of Interest	Safety	
3.1.24	Summary of Infusion-Related Reaction per Preferred Term and MST	Safety	
3.1.25	Summary of On-Study Richter's Transformation and Second Malignancies	Safety	√
3.1.26	Summary of Deaths	Safety	√
3.2.1	Hematology: Summary of Actual Values and Change from Baseline	Safety	√
3.2.2	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities	Safety	√
3.2.2.1	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Male	Safety	√
3.2.2.2	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Female	Safety	√
3.2.2.3	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Age < 65 (years)	Safety	√
3.2.2.4	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Age >= 65 (years)	Safety	√
3.2.2.5	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Race White	Safety	√
3.2.2.6	Hematology: Summary of Treatment-Emergent Laboratory Abnormalities - Race Non-White	Safety	√

Table Number	Title	Analysis Set	Interim
3.2.3	Hematology: Shift from Baseline to worst CTCAE Severity Grade	Safety	√
3.2.4.1	Hematology: Treatment-Emergent Laboratory Abnormalities with >=5% Difference Between Two Groups	Safety	√
3.2.4.2	Hematology: Grade >= 3 Treatment-Emergent Laboratory Abnormalities with >=2% Difference Between Two Groups	Safety	√
3.2.5	Hematology: Exposure-adjusted Incidence Rate of Treatment-Emergent Lab Abnormalities	Safety	√
3.2.6	Serum Chemistry: Summary of Actual Values and Change from Baseline	Safety	√
3.2.7	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities	Safety	√
3.2.7.1	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Male	Safety	√
3.2.7.2	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Female	Safety	√
3.2.7.3	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Age < 65 (years)	Safety	√
3.2.7.4	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Age >= 65 (years)	Safety	√
3.2.7.5	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Race White	Safety	√
3.2.7.6	Serum Chemistry: Summary of Treatment-Emergent Laboratory Abnormalities - Race Non-White	Safety	√
3.2.8	Serum Chemistry: Shift from Baseline to worst CTCAE Severity Grade	Safety	√
3.2.9.1	Serum Chemistry: Treatment-Emergent Laboratory Abnormalities with >=5% Difference Between Two Groups	Safety	
3.2.9.2	Serum Chemistry: Grade >= 3 Treatment-Emergent Laboratory Abnormalities with >=2% Difference Between Two Groups	Safety	
3.2.10	Serum Chemistry: Exposure-adjusted Incidence Rate of Treatment-Emergent Lab Abnormalities	Safety	√
3.2.11	Summary of Liver-related Laboratory Abnormalities	Safety	
3.2.12	Urinalysis: Summary of Actual Values at Baseline	Safety	√
3.2.13	Treatment-Emergent Transaminase Elevations	Safety	√
3.2.14	Time to First Onset and Resolution of Treatment-Emergent Transaminase Elevation	Safety	√
3.2.15	Immunoglobulin: Summary of Actual Values and Change from Baseline	Safety	√

Table Number	Title	Analysis Set	Interim
3.3	Summary of 12-Lead Electrocardiograms at Screening	Safety	√
3.4.1	Oxygen Saturation: Actual Value and Change from Baseline	Safety	
3.4.2	Lowest Oxygen Saturation	Safety	
3.5	Concomitant Medications	Safety	√
4.1.1	Idelalisib Plasma Pharmacokinetic Concentration (ng/mL)	PK	
4.1.2	Idelalisib Metabolite GS-563117 Plasma Pharmacokinetic Concentration (ng/mL)	PK	

Listing Number	Title	Analysis Set	Interim
1.1.1	Screen Failures		√
1.1.2	Eligibility - IRC Assessment		√
1.2	Subject Disposition	ITT	√
1.3	Stratification Factors	ITT	√
1.4	Subjects Excluded From Any	ITT	√
1.5	Important Protocol Deviations	ITT	√
1.6	Subject Demographics and Baseline Characteristics	ITT	√
1.7	CLL Disease History	ITT	√
1.8.1	Prior Therapy	ITT	√
1.8.2	Prior Radiation Therapy	ITT	√
1.9	Medical History	ITT	√
1.10.1	Subject Listing of IDELA Modification (Interruption and Reduction)	Safety	√
1.10.2	Subject Listing of IDELA Dispense and Return with IDELA Adherence	Safety	√
1.10.3	Study Drug (IDELA and Ofatumumab) Administration in Clinic	Safety	√
1.10.4	Study Drug (IDELA) Assignment by IWRS	ITT	√
1.10.5	Continuous Dosing Records of IDELA	Safety	√
2.1.1	Radiographic Assessments of Index Lesions by IRC	ITT	√
2.1.2	Radiographic Assessments of Non-Index Lesions by IRC	ITT	√
2.1.3	Radiographic Assessments of Spleen and Liver by IRC	ITT	√
2.1.4	Overall Radiographic and Clinical Response by IRC	ITT	√
2.1.5	CT/MRI Assessment Dates	ITT	√
2.2.1	CLL Assessment by Physical Examination - Investigator Assessment	ITT	√
2.2.2	CLL Assessment by CT/MRI Scan - Investigator Assessment	ITT	√
2.2.3	Overall CLL Assessment - Investigator Assessment	ITT	√
2.3	Progression-free Survival	ITT	√
2.4	Overall Survival	ITT	√
2.5	Time to First Response and Duration of Response	ITT	√
2.6	Other Efficacy Response Assessment	ITT	√
2.7	Bone Marrow Aspirate and Biopsy	ITT	√
2.8	Organ Biopsy	ITT	√

Listing Number	Title	Analysis Set	Interim
2.9	Functional Assessment of Cancer Therapy: Leukemia (FACT-Leu) Scores	ITT	√
2.10	Karnofsky Performance Status	ITT	√
2.11	EuroQoL Five-Dimension	ITT	√
3.1.1	Laboratory Tests: Hematology	Safety	√
3.1.2	Laboratory Tests: Chemistry	Safety	√
3.1.3	Laboratory Tests: Urinalysis	Safety	√
3.1.4	Laboratory Tests: Immunoglobulin	Safety	√
3.1.5	Laboratory Tests: Hematological Endpoints (ANC)	Safety	√
3.1.6	Laboratory Tests: Hematological Endpoints (ALC)	Safety	√
3.1.7	Laboratory Tests: Hematological Endpoints (Platelet)	Safety	√
3.1.8	Laboratory Tests: Hematological Endpoints (Hemoglobin)	Safety	√
3.1.9	Listing of liver-related Laboratory Abnormalities	Safety	
3.2	Transaminase Elevations	Safety	√
3.3.1	All Adverse Events	Safety	√
3.3.2	Serious Treatment Emergent Adverse Events	Safety	√
3.3.3	TEAEs Leading to Interruption or Modification of IDELA	Safety	√
3.3.4	TEAEs Leading to IDELA Discontinuation	Safety	√
3.3.5	Adverse Events Leading to Death	Safety	√
3.3.6	Summary of Second Malignancies	Safety	√
3.4	All Deaths	Safety	√
3.5	Non-Treatment Emergent Adverse Events	Safety	√
3.6	12-Lead Electrocardiogram	Safety	√
3.7	Body Weight and Oxygen Saturation	Safety	√
3.8	Prior and Concomitant Medications	Safety	√
3.9	Concomitant Therapy Status	Safety	√
3.10	Transfusion Log	Safety	√
3.11	Surgical and Medical Procedures	Safety	√
3.12	Hospitalization	Safety	√
3.13	Pregnancy	Safety	√
3.14	Long-term Follow-up Contact	Safety	√
3.15	Comment	ITT	√

Figure Number	Title	Analysis Set	Interim
1.1.0	Kaplan-Meier Curve of Time to Discontinuation from Study	ITT	
1.1	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment	ITT	√
1.1.1	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
1.1.2	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
1.1.3	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - IgHV Mutated	ITT	√
1.1.4	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - IgHV Unmutated	ITT	√
1.1.5	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - 17p deletion	ITT	√
1.1.6	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - No 17p deletion	ITT	√
1.1.7	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Relapsed Disease Status	ITT	√
1.1.8	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Refractory Disease Status	ITT	√
1.1.9	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Responders	ITT	√
1.1.10	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Non-Responders	ITT	√
1.2	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment	PP	√
1.2.1	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Either)	PP	√
1.2.2	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - del17p/TP53 Mutation (Neither)	PP	√
1.2.3	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - IgHV Mutated	PP	√
1.2.4	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - IgHV Unmutated	PP	√
1.2.5	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - 17p deletion	PP	√
1.2.6	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - No 17p deletion	PP	√
1.2.7	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Relapsed Disease Status	PP	√

Figure Number	Title	Analysis Set	Interim
1.2.8	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Refractory Disease Status	PP	√
1.2.9	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Responders	PP	√
1.2.10	Kaplan-Meier Curve of Progression-free Survival by IRC Assessment - Non-Responders	PP	√
1.3	Forest Plot of Hazard Ratio for Progression-free Survival by IRC Assessment	ITT	√
1.3.1	Forest Plot of Hazard Ratio for Progression-free Survival in the group of 17p/p53 by IRC Assessment	ITT	√
1.4	Kaplan-Meier Curve of Overall Survival	ITT	√
1.4.1	Kaplan-Meier Curve of Overall Survival - del17p/TP53 Mutation (Either)	ITT	√
1.4.2	Kaplan-Meier Curve of Overall Survival - del17p/TP53 Mutation (Neither)	ITT	√
1.4.3	Kaplan-Meier Curve of Overall Survival - IgHV Mutated	ITT	√
1.4.4	Kaplan-Meier Curve of Overall Survival - IgHV Unmutated	ITT	√
1.4.5	Kaplan-Meier Curve of Overall Survival - 17p Deletion	ITT	√
1.4.6	Kaplan-Meier Curve of Overall Survival - No 17p Deletion	ITT	√
1.4.7	Kaplan-Meier Curve of Overall Survival - Relapsed Disease Status	ITT	√
1.4.8	Kaplan-Meier Curve of Overall Survival - Refractory Disease Status	ITT	√
1.4.9	Forest Plot of Hazard Ratio for Overall Survival by IRC Assessment	ITT	√
1.5	Forest Plot of Odds Ratio for Overall Response Rate by IRC Assessment	ITT	√
1.5.1	Forest Plot of Odds Ratio for Overall Response Rate by IRC Assessment	PP	√
1.6	Forest Plot of Odds Ratio for Lymph Node Response Rate by IRC Assessment	ITT	√
1.7	Kaplan-Meier Curve of Duration of Response by IRC Assessment	ITT	√
1.7.1	Kaplan-Meier Curve of Duration of Response by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
1.7.2	Kaplan-Meier Curve of Duration of Response by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
1.7.3	Kaplan-Meier Curve of Duration of Response by IRC Assessment - IgHV Mutated	ITT	√

Figure Number	Title	Analysis Set	Interim
1.7.4	Kaplan-Meier Curve of Duration of Response by IRC Assessment - IgHV Unmutated	ITT	√
1.7.5	Kaplan-Meier Curve of Duration of Response by IRC Assessment - 17p Deletion	ITT	√
1.7.6	Kaplan-Meier Curve of Duration of Response by IRC Assessment - No 17p Deletion	ITT	√
1.7.7	Kaplan-Meier Curve of Duration of Response by IRC Assessment - Relapsed Disease Status	ITT	√
1.7.8	Kaplan-Meier Curve of Duration of Response by IRC Assessment - Refractory Disease Status	ITT	√
1.8	Kaplan-Meier Curve of Time to Response by IRC Assessment	ITT	√
1.8.1	Kaplan-Meier Curve of Time to Response by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
1.8.2	Kaplan-Meier Curve of Time to Response by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
1.8.3	Kaplan-Meier Curve of Time to Response by IRC Assessment - IgHV Mutated	ITT	√
1.8.4	Kaplan-Meier Curve of Time to Response by IRC Assessment - IgHV Unmutated	ITT	√
1.8.5	Kaplan-Meier Curve of Time to Response by IRC Assessment - 17p Deletion	ITT	√
1.8.6	Kaplan-Meier Curve of Time to Response by IRC Assessment - No 17p Deletion	ITT	√
1.8.7	Kaplan-Meier Curve of Time to Response by IRC Assessment - Relapsed Disease Status	ITT	√
1.8.8	Kaplan-Meier Curve of Time to Response by IRC Assessment - Refractory Disease Status	ITT	√
1.9	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment	ITT	√
1.9.1	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - del17p/TP53 Mutation (Either)	ITT	√
1.9.2	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - del17p/TP53 Mutation (Neither)	ITT	√
1.9.3	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - IgHV Mutated	ITT	√
1.9.4	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - IgHV Unmutated	ITT	√
1.9.5	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - 17p deletion	ITT	√

Figure Number	Title	Analysis Set	Interim
1.9.6	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - No 17p deletion	ITT	√
1.9.7	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - Relapsed Disease Status	ITT	√
1.9.8	Waterfall Plot of Best Percent Change from Baseline in SPD by IRC Assessment - Refractory Disease Status	ITT	√
1.11.1	Change from Baseline: FACT-Leu Physical Well-being	ITT	
1.11.2	Change from Baseline: FACT-Leu Social/Family Well-being	ITT	
1.11.3	Change from Baseline: FACT-Leu Emotional Well-being	ITT	
1.11.4	Change from Baseline: FACT-Leu Functional Well-being	ITT	
1.11.5	Change from Baseline: FACT-Leu Additional Concerns	ITT	
1.11.6	Change from Baseline: FACT-Leu Total Outcome Index	ITT	
1.11.7	Change from Baseline: FACT-Leu Total Score	ITT	
1.12.1	Change from Baseline: EQ VAS	ITT	
1.12.2	Change from Baseline: EuroQol Five Dimension Questionnaire Utility Index	ITT	
3.1	Volcano Plot of Any Grade Treatment-Emergent Adverse Events	Safety	√
3.2	Volcano Plot of Any Grade Treatment-Emergent Laboratory Abnormalities	Safety	√
3.3.1	Incidence of Treatment-Emergent Adverse Events of Interest	Safety	
3.3.2	Kaplan-Meier Curve of Time to Onset of First Treatment-Emergent Adverse Event of Interest	Safety	
3.3.3	Prevalence of Treatment-Emergent Adverse Events of Interest	Safety	
3.4.1	Median Over Time: Hemoglobin (g/L)	Safety	√
3.4.1.1	Median Over Time: Hemoglobin (g/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.4.2	Median Over Time: Platelets (x10^9/L)	Safety	√
3.4.2.1	Median Over Time: Platelets (x10^9/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.4.3	Median Over Time: Neutrophils (x10^9/L)	Safety	√
3.4.3.1	Median Over Time: Neutrophils (x10^9/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.4.4	Median Over Time: ALT (U/L)	Safety	√

Figure Number	Title	Analysis Set	Interim
3.4.5	Median Over Time: AST (U/L)	Safety	√
3.4.6	Median Over Time: Lymphocytes (x10^9/L)	Safety	√

Figure Number	Title	Analysis Set	Interim
3.4.7	Median Over Time: Total Bilirubin (umol/L)	Safety	√
3.4.8	Median Over Time: WBC (x10^9/L)	Safety	√
3.4.9	Median Over Time: Triglycerides (mmol/L)	Safety	√
3.4.10	Median Over Time: Serum Glucose (mmol/L)	Safety	√
3.4.11	Median Over Time: IgA (g/L)	Safety	√
3.4.12	Median Over Time: IgG (g/L)	Safety	√
3.4.13	Median Over Time: IgM (g/L)	Safety	√
3.5.1	Change From Baseline: Hemoglobin (g/L)	Safety	√
3.5.1.1	Change From Baseline: Hemoglobin (g/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.5.2	Change From Baseline: Platelets (x10^9/L)	Safety	√
3.5.2.1	Change From Baseline: Platelets (x10^9/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.5.3	Change From Baseline: Neutrophils (x10^9/L)	Safety	√
3.5.3.1	Change From Baseline: Neutrophils (x10^9/L) - Subjects with Abnormality at Baseline and at Least One Post-baseline Measurements	Safety	√
3.5.4	Change From Baseline: ALT (U/L)	Safety	√
3.5.5	Change From Baseline: AST (U/L)	Safety	√
3.5.6	Change From Baseline: Lymphocytes (x10^9/L)	Safety	√
3.5.7	Change From Baseline: Total Bilirubin (umol/L)	Safety	√
3.5.8	Change From Baseline: WBC (x10^9/L)	Safety	√
3.5.9	Change From Baseline: Triglycerides (mmol/L)	Safety	√
3.5.10	Change From Baseline: Serum Glucose (mmol/L)	Safety	√
3.5.11	Change From Baseline: IgA (g/L)	Safety	√
3.5.12	Change From Baseline: IgG (g/L)	Safety	√
3.5.13	Change From Baseline: IgM (g/L)	Safety	√
3.6.1	Kaplan-Meier Curve of Time to Onset of First Episode of Grade 3 and Above Transaminase Elevation	Safety	√
3.6.2	Kaplan-Meier Curve of Time to Resolution of First Episode of Grade 3 and Above Transaminase Elevation	Safety	√