NCT #: NCT02049515

STATISTICAL ANALYSIS PLAN

Protocol IPI-145-12

A Study of IPI-145 and Ofatumumab in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Previously Enrolled in Study IPI-145-07

Protocol Version:	**Amendment 4**
Type of Analysis Plan:	**Final Analysis**
Version:	**1.2**
Date:	**28 Apr 2017**
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		10 MAY 2017

DOCUMENT HISTORY

Version	Date	Author(s)	Brief Summary of Changes
1.0	23 Mar 2015	[redacted]	Original
1.1	01 Apr 2017		Update to Verastem as Sponsor; tabulate and plot only duvelisib group only
1.2	28 Apr 2017		Update to latest protocol amendment

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LIST OF ABBREIVATIONS

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AT	All-Treated
ALT	Alanine Aminotransferase
ANC	Absolute Neutrophil Count
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate Aminotransferase
BID	Twice a day
BOR	Best Overall Response
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CLL	Chronic Lymphocytic Leukemia
CO_2	Bicarbonate
CR	Complete Response
CRi	Complete Response with Incomplete Marrow Recovery
CS	Abnormal and Clinically Significant
CTCAE	Common Terminology Criteria for Adverse Events
DOR	Duration of Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
eDISH	Evaluation of Drug Induced Serious Hepatotoxicity
LDH	Lactate Dehydrogenase
IPI-145	Also known as duvelisib; (S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one
INR	International Normalized Ratio

Abbreviation	Description
IV	Intravenous
IWCLL	International Workshop on Chronic Lymphocytic Leukemia
IWG	International Working Group
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Abnormal but Not Clinically Significant
NED	No Evidence of Disease
ORR	Overall Response Rate
OS	Overall Survival
PD	Progressive Disease
PFS	Progression-Free Survival
PK	Pharmacokinetics
PP	Per-Protocol
PR	Partial Response
PRwL	PR with Lymphocytosis
PT	Preferred Term
PT	Prothrombin Time
RBC	Red Blood Cell
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Stable Disease
SI	Standard International System of Units
SLL	Small Lymphocytic Lymphoma
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
UNK	Unknown
WHO	World Health Organization

1 INTRODUCTION

This is the statistical analysis plan (SAP) for study IPI-145-12, *A Study of IPI-145 and Ofatumumab in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Previously Enrolled in Study IPI-145-07*. This SAP is prepared according to Amendment 4 of the protocol, dated 27 September 2016.

2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to examine the efficacy of duvelisib monotherapy in subjects with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who experienced disease progression after treatment with ofatumumab in Study IPI-145-07 and to examine the efficacy of ofatumumab monotherapy in subjects with CLL or SLL who experienced disease progression after treatment with duvelisib in Study IPI-145-07.

2.2 Secondary Objectives

- To evaluate the safety of duvelisib in subjects with CLL or SLL who experienced disease progression after treatment with ofatumumab in Study IPI-145-07
- To evaluate the safety of ofatumumab in subjects with CLL or SLL who experienced disease progression after treatment with duvelisib in Study IPI-145-07

3 STUDY DESIGN

3.1 Overview

Study IPI-145-12 is a two-arm, open-label, extension study of duvelisib and ofatumumab in patients with CLL/SLL designed to enable subjects who experience disease progression in Study IPI-145-07 to receive the alternative treatment (either duvelisib or ofatumumab) than what they received during study IPI-145-07.

Subjects who meet eligibility criteria will have the option to enroll in this extension study and receive the opposite treatment from what they received in Study IPI-145-07. Both study drugs will be administered in the same manner as defined in Study IPI-145-07.

Subjects who are randomized, receive treatment, and experience disease progression at any time on Study IPI-145-07, will have the option to enroll in this extension study. Following disease progression, subjects will return to the clinic to provide informed consent, assess eligibility and on Day 1 receive their first dose of study drug (either duvelisib or ofatumumab). The first treatment cycle for each treatment arm will be 3 weeks (21±2 days). Subsequent treatment cycles will be 4 weeks (28±4 days).

Subjects who received ofatumumab in study IPI-145-07 will receive duvelisib during this study. Subjects will receive their first dose of duvelisib in clinic on Day 1, initiating Cycle 1 of treatment. These subjects will return for a second clinical visit on Day 8±2. Cycle 1 will be 21 days, with all subsequent cycles 28 days in length. Cycle 2 will have clinic visits on Day 1 and on Day 15±2. Each subsequent cycle (Cycle 3-7, 8, 10, and 12) will have only one clinic visit on Day 1. Subjects may reeived duvelisib until disease progression or unacceptable toxicity.

Subjects assigned to ofatumumab will receive intravenous (IV) treatment according to the approved prescribing information.[1, 2] The initial dose of ofatumumab is 300 mg followed by seven weekly doses of 2000 mg. Thereafter, subjects will receive 2000 mg ofatumumab once every cycle for four cycles or until disease progression or unacceptable toxicity, whichever comes first. Administration of ofatumumab will not exceed the 12 doses (within 7 cycles) as described in the prescribing information.

3.2 Sample Size Consideration

This protocol enables subjects to have access to duvelisib or ofatumumab following treatment with the alternative therapy in IPI-145-07. Therefore, no formal statistical sample size calculation was performed for this study. It is anticipated that approximately 150 subjects may be treated on this protocol. If the sample size for an arm is 75, then a two-sided 95% confidence interval will extend no further than ±12% from an observed ORR.

3.3 Randomization

Not applicable.

3.4 Blinding

This is an open-label extension study for subjects who experience progressive disease while participating in Study IPI-145-07. Enrolled subjects will be assigned to receive the opposite treatment to what they were administered in Study IPI-145-07.

3.5 Planned Analyses

An analysis will be performed using a data cutoff approximately 6 month prior to submission of a new drug application submission for duvelisib to FDA. A final analysis will be performed at when all enrolled subjects have completed participation in the study.

4 ANALYSIS SETS

4.1 All-Treated (AT) Analysis Set

The all-treated (AT) analysis set includes all subjects who receive any amount of study drug (duvelisib or ofatumumab), with treatment group designated according to actual study treatment received. The AT analysis set will be the primary analysis set for efficacy and safety endpoints.

4.2 Per-Protocol (PP) Analysis Set

The per-protocol (PP) analysis set includes all subjects in the AT analysis set who do not violate the terms of the protocol in a way that would significantly affect the study outcome, with treatment group designated according to actual study treatment received. Subjects who meet any of the following criteria may be excluded from this analysis set:

- Do not have documented diagnosis of CLL or SLL within medical records
- ECOG performance status >2
- History of Richter's transformation or prolymphocytic leukemia
- Prior exposure to a PI3K inhibitor (duvelisib arm) or a BTK inhibitor (both arms)
- Receive concomitant prohibited anticancer therapy
- Permanent discontinuation from study drug due to non-compliance

The PP analysis set will be a secondary analysis set for selected efficacy analyses.

5 STUDY ENDPOINTS

5.1 Primary Endpoint

The primary efficacy endpoint is overall response rate (ORR), with overall response defined as the best response of complete response/remission (CR), CR with incomplete marrow recovery (CRi), partial response/remission (PR), or PR with lymphocytosis (PRwL), according to the IWCLL or revised IWG Response Criteria, with modification for treatment-related lymphocytosis.

5.2 Secondary Endpoints

The secondary efficacy endpoints of the study are:

- Treatment-Emergent Adverse Events (TEAEs) and changes in laboratory values
- Duration of Response (DOR), defined as the time from the first documentation of response to the first documentation of progressive disease (PD) or death due to any cause
- Progression-Free Survival (PFS), defined as the time from the first dose of study treatment to the first documentation of PD or death from any cause

6 GENERAL STATISTICAL METHODS AND DATA HANDLING

6.1 General Methods

Summary statistics will be presented for the duvelisib treatment group, unless stated otherwise.

Unless otherwise specified, descriptive statistics for continuous data will include the number of subjects with data to be summarized (n), mean, standard deviation, median, and minimum and maximum. The same number of decimal places as in the raw data will be presented when reporting the minimum and maximum, one more decimal place than the raw data will be presented when reporting mean and median, and 2 more decimal places than the raw data will be presented when reporting standard deviation.

Descriptive statistics for categorical/qualitative data will include frequency counts and percentages. The total number of subjects in the treatment group will be used as the denominator for percent calculations, unless stated otherwise. All percentages will be presented with one decimal, unless otherwise specified. Percentages equal to 100 will be presented as 100, and percentages will not be presented for zero frequencies.

Descriptive statistics associated with time-to-event analyses will include the number of events, the number of subjects censored, 25% quartile, median, 75% quartile, and corresponding 95% confidence interval for median. These statistics will be presented for all time-to-event analyses, unless stated otherwise.

For listings broken down by center and treatment arm, site (center) number will be ordered by country.

6.2 Handling of Missing Data

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

6.2.1 Handling of Missing Dates/Months/Years for Adverse Events

Adverse events (AEs) with incomplete onset dates will be handled as follows for the sole purpose of determining treatment emergence (TEAE is defined in Section 7.3.1):

- If the start/end date of an AE is partially missing, the date will be compared as far as possible with the date of the start of administration of study drug and the date of last dose of study drug plus 30 days. The AE will be assumed to be treatment emergent if it cannot be definitively shown that the AE did not occur or worsen during the treatment-emergent period (worst case approach). The detailed algorithm will be specified in ADaM specifications.
- If the start date is completely missing, an AE will be considered treatment-emergent unless the stop date is before study drug administration.
- If the dose start date is missing for a subject at a data-cut, all AEs of the subject will be considered treatment-emergent.

The original partial or missing date will be shown in all listings of AEs.

6.2.2 Handling of Missing Dates/Months/Years for Concomitant Medications

Prior or concomitant medications with incomplete start dates will be handled as follows for the sole purpose of determining whether a non-study medication is a concomitant medication:

- If the start/stop date of a medication is partially missing, the date will be compared as far as possible with the date of the start of administration of study drug and the date of last dose of study drug plus 30 days. The medication will be assumed to be concomitant if it cannot be definitively shown that the stop date is before the start of administration of study drug, or the start date is more than 30 days after the last date of administration of study drug. The detailed algorithm will be specified in ADaM specifications.
- If the start/stop dates are completely missing, a medication will be considered concomitant.
- If the dose start date is missing for a subject at a data-cut, all non-study medications of the subject will be considered concomitant.

The original partial or missing date will be shown in listings of all non-study medications.

6.2.3 Handling of Missing Dates/Months/Years for Disease History and Prior Therapies

For the purpose of calculating the duration from initial diagnosis, most recent relapse/refractory diagnosis or most recent prior therapy to first dose, partial/missing dates for diagnosis and last prior therapy completion will be imputed as follows:

- If both date and month are missing and the year is prior to the year of screening, the imputed date and month will be 01 July.
- If both date and month are missing and the year is the same as the year of screening, the imputed date will be the middle point between 01 Jan of the year and the screening date. If the middle point falls between two dates, the first of the two dates will be used.
- If date is missing and the month and year are prior to the month and year of screening, the imputed date will be 15th day of the month.
- If date is missing and the month and year are the same as the month and year of screening, the imputed date will be the middle point between the first date of the month and the screening date. If the middle point falls between two dates, the first of the two dates will be used.
- No imputation will be performed if the year is missing.

6.3 Multiple Comparisons/Multiplicity Adjustment

Not applicable since no formal statistical testing will be performed.

6.4 Adjustments for Covariates

Not applicable.

6.5 Subgroups

ORR and PFS will be examined in the following subgroups, if sample sizes allow the analyses:

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

TEAEs (All Causalities) and TEAEs (Treatment-Related) will be examined in the following subgroups:

- Gender (Male or Female)
- Age group (<65 or ≥65)
- Race (White or Non-White)
- Baseline ECOG performance status (0 or 1 versus 2)

More details will be specified in Sections 7.2.1, 7.2.2 and 7.3.1.

6.6 Visit Windows

All data will be categorized based on the scheduled visit at which it was collected. These visit designators are predefined values that appear as part of the visit tab in the eCRF. There will be no additional analysis windowing done based on the assessment date.

6.7 Unscheduled Visits

Unscheduled visits will not be included in by-visit summary tables, unless otherwise specified. For laboratory tests, data from unscheduled visits will be included in listings and summaries of maximum changes from baseline, and the best or worst post-baseline values. For endpoints based on disease status assessment, data from unscheduled assessments will be included in the derivation and analyses of the endpoints.

6.8 Baseline Values

Unless otherwise specified, the baseline value is defined as the value collected at the time closest to, and prior to, the start of study drug administration. Values collected at unscheduled visits prior to the start of the study drug administration will be included in the calculation of baseline values.

6.9 Computing and Coding Standards

Activities will be performed using the following tools:

Table, listing, and figure production	SAS Version 9.2 or higher
Coding	
Adverse Events	MedDRA Version 16.1 or higher

Medical Histories	MedDRA Version 16.1 or higher
Prior and Concomitant Medications	WHODrug Version September 2013
Grading	
AEs	CTCAE Version 4.03
Labs	CTCAE Version 4.03

7 STATISTICAL ANALYSES

7.1 Study Subjects

7.1.1 Disposition of Subjects

The disposition of subjects will include the number dosed based on the AT analysis set.

An end-of-treatment disposition (still on treatment vs discontinued from treatment) will be provided based on the AT analysis set. The primary reason for treatment discontinuation will be included in the table. A listing of these subjects will also be provided, broken down by reatment arm.

An end-of-study disposition (still on study vs discontinued from study) will also be provided based on the AT analysis set. The primary reason for study discontinuation will be included in the table. A listing of these subjects will also be provided, broken down by treatment arm.

7.1.2 Protocol Deviations

Protocol deviations will be assessed during monitoring visits and by data review. At minimum, the following categories of study conduct or data will be assessed for potential protocol deviations: entry criteria, concomitant medications, dosing records, laboratory results, visit schedule and procedures. Protocol deviations will be categorized as major or minor prior to data release for the final analysis of the primary endpoint. A summary table of the protocol deviations will be provided for the AT analysis set. A listing of all protocol deviations will be provided, broken down treatment arm.

7.1.3 Demographic and Other Baseline Characteristics

Demographic variables will be summarized based on AT analysis set. The variables will include age, age group (<65 versus >=65), sex, race, ethnicity, height, and weight.

7.1.4 Disease History

Disease history will be summarized based on the AT analysis set. The variables will include diagnosis (CLL or SLL), risk factors used for randomization in IPI-145-07 study that are reported on eCRF (high risk cytogenetics [17p deletion: presence vs absence], refractory/early relapse to purine analog based treatment [yes vs no], grade 4 cytopenia(s) [presence vs absence]), years from initial diagnosis to first dose, months from most recent relapse/refractory diagnosis to first dose, stage at initial diagnosis, type of prior treatment, current stage, Binet/Rai stage, and baseline lymphocytes.

The durations to be summarized are defined as follows:

- Years from initial diagnosis to first dose will be calculated as (date of first dose – date of initial diagnosis + 1)/365.25.
- Months from most recent relapse/refractory diagnosis to first dose will be calculated as (date of first dose – date of most recent relapse/refractory diagnosis + 1)/ (365.25/12).

The imputation of partial/missing dates is described in Section 6.2.3.

7.1.5 Prior Therapies

Prior therapies (eg, prior to 145-07) will be summarized based on the AT analysis set. The variables will include number of prior systemic therapies (summarized as a continuous variable and as a categorical variable), months from most recent prior therapy to first dose, number and percentage of subjects with prior radiotherapy, and number and percentage of subjects with prior surgery related to primary diagnosis.

The durations to be summarized are defined as follows.

- Months from most recent prior therapy (again, prior to dosing in study 145-07) to first dose will be calculated as (date of first dose – stop date of most recent systemic therapy, prior irradiation or prior surgery +1)/ (365.25/12).

The imputation of partial/missing dates is described in Section 6.2.3. A by-subject listing will be presented for prior systemic therapy.

7.1.6 Medical History

Medical history will be summarized based on the AT analysis set.

Medical history will be summarized by system organ class (SOC) and preferred term (PT) using the number and percentage of subjects who had at least one occurrence of an SOC or PT. The summary will be sorted alphabetically in SOC and by decreasing frequency of PT in the duvelisib arm within an SOC.

7.1.7 Prior and Concomitant Medications

Medications will be considered as prior if they stopped before the date of first dose of study drug.

Medications will be considered concomitant if they were taken at any time between the date of first dose of study drug and 30 days after the date of last dose of study drug, inclusive. If the start date or end date of a medication is completely or partially missing, refer to Section 6.2.2 for the algorithm to determine whether a medication is concomitant.

Prior medications and concomitant medications will be summarized separately. Both summaries will be based on the AT analysis set.

Medications will be summarized by ATC level 1, ATC level 2, and preferred drug name. The summary will be sorted by decreasing frequency in ATC level 1, ATC level 2 and preferred drug name in the duvelisib arm. A subject taking the same drug multiple times will only be counted once.

A listing will be provided for all non-study medications taken on the study. An identifier will be provided to show if a medication is prior or concomitant. Medications that started more than 30 days after the last dose of study drug will be identified as post-treatment.

7.1.8 Exposure to Study Drug

Extent of exposure will be summarized based on the AT analysis set.

Extent of exposure will be summarized for the following variables:

- Duration (weeks): (date of last dose – date of first dose + 1) divided by 7
- Number of cycles started (continuous and categorical)
- Relative dose intensity, defined as 100% x (total dose received)/ (planned cumulative dose for the duration of treatment)
- Number and percentage of subjects with a dose reduction
- Number and percentage of subjects with a dose interruption
- Number and percentage of subjects with study drug discontinued

7.2 Efficacy Analyses

ORR, DOR, and PFS will be derived from investigator assessment.

AT analysis set will be the primary analysis set for all efficacy analyses. If analyses are performed on more than one analysis set, the analyses on the AT analysis set will be considered primary. No treatment comparison between the two arms will be performed and only efficacy endpoints for the duvelisib arm will be tabulated and plotted. Data for both treatment arms will be included in data listings.

7.2.1 Analyses of Primary Endpoint

7.2.1.1 Overall Response Rate

ORR will be derived from best overall response (BOR), which is defined as the best time point response that a subject achieves during the course of the study, with the response ranked according to the following order (from best to worst): CR>CRi>PR>PRwL>SD>PD (CRi applies to CLL only).

The estimated ORR (percent of subjects with a BOR of CR, CRi, PR or PRwL) and a 2-sided 95% CI will be provided. The 95% CI will be calculated using exact binomial method. Number and percent of subjects with BOR in each of the response categories (CR, CRi, PR, PRwL, SD, PD) will also be presented. All subjects in the analysis set will be included in the denominator in the calculation of the percentage for each response category or ORR.

Analysis of ORR using the PP analysis set will be provided as a sensitivity analysis.

Subgroup analyses will be performed for ORR using the subgroups specified in Section 6.5.

7.2.2 Analyses of Secondary Efficacy Endpoints

The analysis of secondary efficacy endpoint, Duration of Response (DOR) and Progression Free Survival (PFS), will be descriptive only.

7.2.2.1 Duration of Response (DOR)

DOR will be presented using the Kaplan-Meier method based on all treated subjects with a documentation of response (i.e., CR, CRi, PR, or PRwL) as determined by investigator assessment. The censoring rule will be the specified in Appendix A. The Kaplan-Meier estimates of survival curves and number of subjects with events, types of events (progression or death before progression), number of subjects censored, number of subjects for each reason of censoring, estimates and 95% confidence intervals for the 25th percentile, median, and 75th percentile for DOR will be presented (if estimable).

Analysis of DOR using the PP analysis set will be provided as a sensitivity analysis.

7.2.2.2 Analyses of PFS

PFS will be presented using the Kaplan-Meier method based on all treated subjects with a documentation of response (i.e., CR, CRi, PR, or PRwL) as determined by investigator assessment. The censoring rule will be the specified in Appendix A. The Kaplan-Meier estimates of survival curves and number of subjects with events, types of events (progression or death before progression), number of subjects censored, number of subjects for each reason of censoring, estimates and 95% confidence intervals for the 25th percentile, median, and 75th percentile for PFS will be presented (if estimable).

PFS will be plotted using the Kaplan-Meier method. The plot will include the number of subjects at risk over time.

Analysis of PFS using the PP analysis set will be provided as a sensitivity analysis.

7.3 Safety Analyses

All safety analyses will be performed using the AT analysis set.

7.3.1 Adverse Events

Adverse events will be coded using MedDRA Version 16.1 or higher. The Grade of the AE will be assessed according to the NCI-CTCAE Version 4.03. If an AE is not included in the NCI-CTCAE Version 4.03, the Grade of the AE will be assessed according to the protocol, Section ***8.2.1.2***.

AEs will be summarized by MedDRA system organ class (SOC) and preferred term (PT), or PT only. For summary tables by SOC and PT, SOC will be sorted alphabetically and PT will be sorted by decreasing frequency in the duvelisib arm within each SOC. For summary tables by PT only, PT will be sorted by decreasing frequency in the duvelisib arm.

If multiple AEs of the same PT occur within a subject, only the maximum grade observed for this PT will be used in summary of AEs by grade, the subject will be counted only once in the number of subjects for this PT and only once for the number of subjects for the SOC to which this PT belongs.

A treatment-emergent AE (TEAE) is defined as any AE that emerges or worsens in the period from the first dose of study treatment to 30 days after the last dose of study treatment. The onset date of an AE will be compared to the first dose date and the last dose date plus 30 days to determine whether the AE is treatment-emergent or not. If the onset date of an AE is completely or partially missing, refer to Section 6.2.1 for the algorithm to determine whether an AE is treatment emergent.

An overview TEAE summary table will be provided, which will include the number of AEs and the number of subjects with AEs in selected categories. In addition, TEAEs will be summarized for the following categories, and will be tabulated by SOC and PT, unless otherwise specified.

- Treatment-emergent AEs (All Causalities)
- Treatment-emergent AEs (Treatment-Related)
- Treatment-emergent AEs (All Causalities, by maximum grade)
- Treatment-emergent AEs (Treatment-Related, by maximum grade)
- Grade 3 or higher treatment-emergent AEs (All Causalities)
- Grade 3 or higher treatment-emergent AEs (Treatment-Related)
- Treatment-emergent SAE (All Causalities)
- Treatment-emergent SAE (Treatment-Related)
- Treatment-Emergent AEs Resulting in Discontinuation of Study Drug
- Treatment-Emergent AEs Resulting in dose hold or reduction (number of subjects with hold, reduction, hold or reduction will be displayed)
- Treatment-Emergent AEs Resulting in Death
- Treatment-Emergent AEs by PT (All Causalities)
- Grade 3 or higher treatment-emergent AEs by PT (All Causalities)

A by-subject listing of the following AE categories will be presented.

- All AEs (TEAEs will be flagged)
- All SAEs (TEAEs will be flagged)
- Treatment-Emergent AEs Resulting in Discontinuation of Study Drug
- Treatment-Emergent AEs Resulting in Death

Treatment-emergent AEs (All Causalities) and Treatment-emergent AEs (Treatment-Related) will also be tabulated in each subgroup specified in Section 6.5.

7.3.2 Laboratory Data

Laboratory tests will be reported separately for hematology/coagulation, blood chemistry, and urinalysis.

For the purposes of presentation in both tables and listings, the following laboratory test results will be converted to the International System of Units (SI) before presentation: sodium, potassium, chloride, bicarbonate (or CO_2), albumin, total protein, creatinine, blood urea nitrogren(BUN), lipase, amylase, uric acid, calcium, phosphorus, magnesium, glucose, lactate dehydrogenase(LDH), serum ALT, serum AST, total and direct bilirubin, and alkaline phosphatase, red blood cell (RBC) count, hemoglobin, hematocrit, platelets, white blood cell count with 5-part differential performed manually or by flow cytometry (for an absolute neutrophil count [ANC], lymphocyte count, neutrophils, lymphocytes, monocytes, basophils, and eosinophils), prothrombin time(PT), activated partial thromboplastin time(aPTT), international normalized ratio (INR) etc.

If a laboratory test value is reported using a non-numeric qualifier (e.g., less than [<] a certain value, or greater than [>] a certain value), the given numeric value will be used in the summary statistics, ignoring the non-numeric qualifier.

For laboratory tests with NCI-CTCAE grades, a shift table from baseline grade to the maximum post-baseline grade will be provided. Laboratory tests with bi-directional grades (e.g., Hyperglycemia and Hypoglycemia) will be presented separately for each direction within the shift table.

Listings will be provided for all laboratory test results and for laboratory test results grade 3 and higher. A listing of subjects with ALT or AST >3xULN with simultaneous total bilirubin >2xULN will be presented, where ULN stands for upper limit of normal.

7.3.3 Vital Signs

The actual values of vital sign parameters, including temperature, heart rate, weight and systolic and diastolic blood pressure, will be presented in a by-subject listing.

7.3.4 Electrocardiogram (ECG)

The ECG categories will be summarized for baseline and for each visit. The categories include normal, abnormal, NCS (abnormal but not clinically significant) and abnormal CS (abnormal and clinically significant).

7.3.5 Physical Examination

A full physical examination will be performed during Screening and focused physical examination will be performed every 2 cycles and every 6 cycles starting Cycle 24. A list of abonormal findings will be provided.

7.3.6 Eastern Cooperative Oncology Group (ECOG)

ECOG Performance Status will be assessed during Screening, every 2 cycles and every 6 cycles starting Cycle 24. A listing of all the ECOG performance status will be provided.

7.3.7 Concomitant Medications and Procedures

Please refer to Section 7.1.7 for the definition and summary of concomitant medications.

Concomitant procedures will not be summarized. A by-subject listing will be presented.

7.3.8 Pregnancy

A listing of Serum Pregnancy Test for woman with child-bearing potential will be provided.

8 CHANGES IN PLANNED ANALYSES FROM PROTOCOL

Due to the very small number of subjects (n=8) in the ofatumab treatment arm only results for the duvelisib treatment arm will be tabulated and plotted. Subjects from both treatment arms will be present in the data listings.

9 REFERENCES

None.

10 APPENDICES

A. PFS censoring rule

Censoring of PFS will be performed as detailed in the table below.

Primary PFS Censoring / Event Methodology

Situation	Date of Event or Censoring	Outcome
No adequate baseline disease status assessment	Date of first dose	Censored
No adequate post-baseline disease status assessment unless death occurs prior to first post-baseline assessment	Date of first dose + 1	Censored
No documented progression or death before data cutoff	Date of last adequate disease status assessment	Censored
Documented progression with ≤1 missing scheduled disease status assessment before progression	Date of the earliest assessment that results in a finding of unequivocal progression	Event
Death before progression being documented with ≤1 missing scheduled disease status assessment before death	Date of death	Event
Documented progression or death following a long gap between adequate disease status assessments (eg, 2 or more consecutive missed scheduled disease status assessments)	Date of last adequate disease status assessment before the gap	Censored
New anticancer treatment or procedure started before documented progression	Date of last adequate disease status assessment prior to new anticancer treatment	Censored

Note: Disease status assessment includes CT scans (chest, abdomen and pelvis), bone marrow aspirate and/or biopsy (may not be required of all subjects at all scheduled disease status assessments), CBC and differential count, focused physical examination, disease related constitutional symptoms for disease assessment, and ECOG performance status. An adequate disease status assessment is any disease status assessment for which the investigator review is able to arrive at a disease status (eg, CR, CRi, PR, PRwL, SD, and PD) per protocol-defined criteria.