Protocol Registration Receipt
05/29/2014

Grantor: CDER IND/IDE Number: 11719 Serial Number: 049

HuMax-CD20 in B-Cell Chronic Lymphocytic Leukemia (B-CLL) Patients Failing Fludarabine and Alemtuzumab

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00349349

Purpose

The purpose of this study is to determine whether HuMax-CD20 (ofatumumab) is effective in the treatment of patients failing both fludarabine and alemtuzumab.

Condition	Intervention	Phase
Leukaemia, Lymphocytic, Chronic	Drug: ofatumumab	Phase 2

Study Type: Interventional

Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Safety/Efficacy Study

Official Title: A Single-arm, International, Multi-center Trial of HuMax-CD20, a Fully Human Monoclonal Anti-CD20 Antibody, in Patients With B-cell Chronic Lymphocytic Leukemia Who Have Failed Fludarabine and Alemtuzumab

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as Assessed by an Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines [Time Frame: Start of treatment (Week 0 of Visit 2) until Week 24] [Designated as safety issue: No]

  Par. with complete remission (CR), nodular partial remission (nPR), and partial remission (PR) were classified as responders, while those with stable disease (SD) and progressive disease (PD) were classified as non-responders. Per the NCIWG guideline (1996): CR; no lymphadenopathy/hepatomegaly/splenomegaly/constitutional symptoms, normal hematology, bone marrow sample as normocellular for age, <30% lymphocytes (LC), no lymphoid nodule; PR: a >=50% decrease in LC/lymphadenopathy; nPR: persistent nodules in bone marrow; PD: new lesion or increase by >=50% from baseline; SD: no CR, PR, or PD.

Secondary Outcome Measures:

- Duration of Response [Time Frame: Start of treatment (Week 0 of Visit 2) until Week 24] [Designated as safety issue: No]

  Duration of response is defined as the time from the initial response (first visit at which response is observed) to progression or death. If the participant had progression between scheduled visits, no progression at the end of the trial, treatment discontinuation for undocumented progression, treatment discontinuation for toxicity or other reason, new anti-cancer treatment, and experienced death or progression after two or more missed visits in a row the endpoint was censored.
- Progression-Free Survival (PFS) [Time Frame: Start of treatment (Week 0 of Visit 2) until Week 24] [Designated as safety issue: No]

  PFS is defined as the time from randomization until progression/death. Per the IRC, if the participant had progression between scheduled visits, died before the first assessment, or died between adequate visits, the endpoint was considered progressed. If there was no progression at the end of the trial, treatment discontinuation for undocumented progression, treatment discontinuation for toxicity/other reason, new anti-cancer treatment, and death/progression after 2 or more missed visits in a row, the endpoint was censored. Clinical progression is not considered as progression endpoint.
- Time to Next Chronic Lymphocytic Leukemia (CLL) Treatment [Time Frame: Time from randomization (Week 0 of Visit 2) until the time of first administration of a CLL treatment other than ofatumumab (assessed for a median of 8.7 weeks currently [or up to 13.3 months])] [Designated as safety issue: No]

  Time to next chronic lymphocytic leukemia (CLL) treatment is defined as the time from treatment allocation/randomization (Visit 2) until the time of the first administration of the next CLL treatment other than ofatumumab (or HuMaxCD20, a fully human monoclonal antibody to CD20 that is expressed on the surface of B-cells).
- Overall Survival [Time Frame: Start of randomization (Week 0 of Visit 2) until death (up to a median of 17.1 weeks)] [Designated as safety issue: No]

  OS is defined as the time from allocation to death. OS will also be subgrouped for responders and non-responders.
- Percent Change From Baseline to Week 7 in Peripheral CD5+CD19+ Cell Counts [Time Frame: Baseline (Visit 2) until Week 7 (Visit 9)] [Designated as

safety issue: No]

The peripheral blood for each participant was collected and analyzed for CD5+CD19+ cell counts. CD is "cluster of differentiation," is a cell surface marker for immunophenotyping, and, in this case, is a surrogate for B cell malignancy (indicates malignant B cells). Percent change from Visit 2 (Week 0, Baseline) = (value at Week 7 minus value at Week 0 divided by value at Week 0) x 100.

- Percent Change From Baseline to Week 7 in Peripheral CD5+CD20+ Cell Counts [Time Frame: Baseline (Visit 2) until Week 7 (Visit 9)] [Designated as safety issue: No]

  The peripheral blood for each participant was collected and analyzed for CD5+CD20+ cell counts. CD is "cluster of differentiation," is a cell surface marker for immunophenotyping, and, in this case, is a surrogate for B cell malignancy (indicates malignant B cells). Percent change from Visit 2 (Week 0, Baseline) = (value at Week 7 minus value at Week 0 divided by value at Week 0) x 100.
- Median Percent Change of Tumor Size (Sum of Products Dimensions [SPD]) From Baseline (Visit 2) to Week 24 (Visit 14) [Time Frame: Baseline (Visit 2) until Week 24 (Visit 14)] [Designated as safety issue: No]

  Tumor size and change in tumor size will be measured by the absolute value of and the percent change in the sum of products of the diameters of the largest abnormal lymph nodes from Baseline to Week 24 (Visit 14). Percent change from Visit 2 (Baseline, Week 0) = (value at Week 24 minus value at Week 0 divided by value at Week 0) x 100.
- Number of Participants With Complete Resolution of Constitutional Symptoms at Week 24 [Time Frame: Baseline (Visit 2) and Week 24] [Designated as safety issue: No]

  Participants with complete resolution of constitutional symptoms were those in whom no constitutional symptoms, such as night sweats, weight loss, and fever or extreme fatigue, were observed.
- Number of Participants With Complete Resolution of Lymphadenopathy [Time Frame: Baseline (Visit 2) to end of study (up to Week 24)] [Designated as safety issue: No]

  Participants with complete resolution of lymphadenopathy (disease involving the lymph nodes) were defined as those in whom all observed lymph nodes were of normal size (all nodes <1 centimeters) as determined by physical examination assessed by the investigator. All palpable lymph node sizes were recorded.
- Number of Participants With Improvement on the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale at Week 24 [Time Frame: Baseline (Visit 2) and Week 24] [Designated as safety issue: No]

  ECOG performance status is a measure of the participant's ability to carry out activities of daily living on 6-point scale (0=fully active, 1=restricted in physically activity, ambulatory, 2=ambulatory [>50% of waking hours], 3=capable of only limited self care, 4=completely disabled, 5=Dead). Improvement in ECOG performance status is defined as a decrease from baseline by at least one score on the ECOG scale.
- Number of Participants Who Were Positive, Negative, or Had Missing Data for the Indicated Fluorescence in Situ Hybridization (FISH) Prognostic Factors at Screening [Time Frame: Screening (Visit 1, <=14 days prior to Visit 2)] [Designated as safety issue: No]

  The number of participants (par.) who were positive, negative, or had missing data for the following prognostic factors indicative of altered responsiveness to treatment and/or survival was measured: 17p-, 11q-, +12q, 6q-, 13q-. Par. were assessed by FISH for these chromosomal abnormalities known tobe prognostic for time to treatment and survival when detected at diagnosis. Par. were categorized by the chromosomal abnormality detected: 17 p deletion, 11q deletion (but not 17 p deletion), 12 q trisomy (but not 17 p or 111q deletion), 13q deletion only, and no chromosomal abnormalities found.

- Number of Participants With Improvement in Hemoglobin [Time Frame: Baseline (Visit 2) to Week 28] [Designated as safety issue: No]
  The number of participants (par.) who had improvement in hemoglobin levels >=11 grams (g)/deciliter (dl) (6.8 millimoles/liter) or 50% improvement over baseline was measured.
- Number of Participants With Improvement in Thrombocytopenia (Thromb.) [Time Frame: Baseline (Visit 2) to Week 28] [Designated as safety issue: No]
  Improvement in thromb. is defined as a decrease from Visit 2 by >=1 National Cancer Institute Common Terminology Criteria (NCI CTC) grade. Thromb. is defined as low platelet counts resulting from refractory CLL, damage from prior treatment, advanced age, or reduced bone marrow function and can be considered as an adverse condition. Adverse events (AEs) such as thromb. in a cancer indication are graded on a scale determined by the NCI called the NCI CTC: lowest, grade 1; highest, grade 5 (death). Changes in this grading can assess improvements or declines in the severity of the AE.
- Number of Participants With Complete Resolution of Hepatomegaly [Time Frame: Baseline (Visit 2) until Week 24] [Designated as safety issue: No]
  Participants with complete resolution of enlarged liver (hepatomegaly) were defined as those with an enlarged palpable liver at baseline followed by the absence of hepatomegaly post- baseline (i.e., the liver was of normal size). Liver size was assessed by physical examination and documented as "centimeters" under the costal margin with relative changes in spleen size in 1 dimension calculated based on palpated numeric measurements (as per the 1996 NCIWG guidelines).
- Number of Participants With Improvement in Neutropenia [Time Frame: Baseline (Visit 2) to Week 28] [Designated as safety issue: No]
  Low levels of neutrophils (neutropenia) may increase the risk of developing serious infections and may be considered an adverse condition and evaluated on the NCI CTC with a grade. Improvement in neutropenia is defined as a decrease from Visit 2 (baseline) by at least one NCI CTC grade. Improvement is defined as a decrease from Visit 2 by at least one NCI CTC grade.
- Number of Participants With Complete Resolution of Splenomegaly [Time Frame: Baseline (Visit 2) until Week 24] [Designated as safety issue: No]
  Participants with complete resolution of enlarged spleen (splenomegaly) were defined as those with an enlarged palpable spleen at baseline followed by the absence of splenomegaly post-baseline (i.e., the spleen was of normal size). Spleen size was assessed by physical examination and documented as "centimeters" under the costal margin with relative changes in spleen size in 1 dimension calculated based on palpated numeric measurements (as per the 1996 NCIWG guidelines).
- Number of Participants Who Experienced Any Adverse Event [Time Frame: From first infusion (Visit 2/Week 0) to Visit 21 (Month 24 of follow-up [up to Month 48]) or time of withdrawal (treatment and follow-up)] [Designated as safety issue: Yes]
  An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which did not necessarily have a causal relationship with the treatment. A list of AEs experienced in the study with a frequency threshold of 5% can be found in the AE section of this results record.
- Cmax and Ctrough at Dose 1 (Visit 2, Week 0), Dose 8 (Visit 9, Week 7), and Dose 12 (Visit 14, Week 24) [Time Frame: Visit 2 (Week 0), Visit 9 (Week 7), and Visit 14 (Week 24)] [Designated as safety issue: No]
  Cmax is defined as the maximum concentration of drug in serum samples. Ctrough is defined as the trough serum concentration (measured concentration at the end of a dosing interval [taken directly before the next administration]). No drug was present before the first infusion; therefore, there are no Ctrough results for Dose 1
- AUC (0-inf) and AUC(0-tau) at Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24) [Time Frame: Visit 9 (Week 7) and Visit 14 (Week 24)] [Designated as safety issue: No]
  AUC is defined as the area under the ofatumumab concentration-time curve as a measure of drug exposure. AUC(0-inf) is AUC from the start of infusion

extrapolated to infinity. AUC(0-tau) is AUC from the start of infusion over the dosing interval.

- Half-life (t1/2) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24) [Time Frame: Visit 9 (Week 7) and Visit14 (Week 24)] [Designated as safety issue: No]
  Half-life (t1/2) is defined as the terminal half-life and is the time required for the amount of drug in the body to decrease by half.
- Clearance (CL) After Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24) [Time Frame: Visit 9 (Week 7) and Visit 14 (Week 24)] [Designated as safety issue: No]
  CL is the clearance of drug from serum, which is defined as the volume of serum from which the drug is cleared per unit time.
- Volume of Distribution at Steady State (Vss) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24) [Time Frame: Visit 9 (Week 7) and Visit 14 (Week 24)] [Designated as safety issue: No]
  Vss is defined as the volume of distribution at steady state of ofatumumab.

Enrollment: 223
Study Start Date: June 2006
Study Completion Date: June 2012
Primary Completion Date: May 2008

Arms	Assigned Interventions
Experimental: ofatumumab Anti-CD20 antibody therapy	Drug: ofatumumab Intravenous infusion

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

1. Tumor cell phenotype consistent with B-CLL
2. Patients with active B-CLL and with an indication for treatment
3. Failing at least one fludarabine-containing treatment regimen
4. Failing at least one alemtuzumab-containing treatment regimen
5. ECOG Performance Status of 0, 1, or 2
6. Life expectancy of at least 4 months

Exclusion Criteria:

1. Previous treatment with alemtuzumab within 6 weeks prior to Visit 2
2. Previous autologous stem cell transplantation within 6 months prior to Visit 2
3. Allogeneic stem cell transplantation
4. Radioimmunotherapy

Contacts and Locations

Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Results Publications:

Wierda WG, Kipps T, Mayer J, Stilgenbauer S, Williams CD, Hellmann A, Robak T, Furman R, Hillmen P, Trneny M, Dyer M, Padmanabhan S, Piotrowska M, Kozak T, Chan G, Davis R, Losic N, Russell C, Wilms J, Osterborg A. Ofatumumab as single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia. [J Clin Oncol]. 2010;28(10):1749-1755.

Other Publications:

Wierda WG, Padmanabhan S, Chan GW, Gupta IV, Lisby S and Osterborg A . Ofatumumab is active in patients with fludarabine-refractory chronic lymphocytic leukemia irrespective of prior rituximab: Results from the phase II international study. [Blood]. 2011;118(19):5126-5129.

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	111773
	Hx-CD20-406 [Genmab]
Health Authority:	United States: Food and Drug Administration

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Study Results

Participant Flow

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab intravenous (iv) infusion was initiated at 300 milligrams (mg), followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The independent endpoint review committee (IRC) classified these participants as double refractory (DR), defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as bulky fludarabine refractory (BFR), defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other," defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Overall Study

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Started	95	112	16
Completed	42	50	10
Not Completed	53	62	6
Adverse Event	5	6	2

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Withdrawal by Subject	5	2	1
Withdrawn due to Disease Progression	27	37	1
Death	13	10	1
Other Treatment Selected	2	0	0
Participant Reduced General Condition	0	1	0
Physician Decision	1	2	1
No Response	0	3	0
New Malignancy (Bladder Cancer)	0	1	0

Baseline Characteristics

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as

	Description
	BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Baseline Measures

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other	Total
Number of Participants	95	112	16	223
Age, Continuous [units: Years] Mean (Standard Deviation)	63.2 (8.4)	64.4 (9.3)	64.5 (7.4)	63.9 (8.8)
Gender, Male/Female [units: Participants]				
Female	24	31	5	60
Male	71	81	11	163
Race/Ethnicity, Customized [units: participants]				
Asian	1	0	1	2
Black or African American	2	1	0	3
Hispanic or Latino	1	0	0	1
White	88	111	15	214

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other	Total
Arab	1	0	0	1
Yemenite	1	0	0	1
Middle Eastern	1	0	0	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as Assessed by an Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines
Measure Description	Par. with complete remission (CR), nodular partial remission (nPR), and partial remission (PR) were classified as responders, while those with stable disease (SD) and progressive disease (PD) were classified as non-responders. Per the NCIWG guideline (1996): CR; no lymphadenopathy/hepatomegaly/splenomegaly/constitutional symptoms, normal hematology, bone marrow sample as normocellular for age, <30% lymphocytes (LC), no lymphoid nodule; PR: a >=50% decrease in LC/lymphadenopathy; nPR: persistent nodules in bone marrow; PD: new lesion or increase by >=50% from baseline; SD: no CR, PR, or PD.
Time Frame	Start of treatment (Week 0 of Visit 2) until Week 24
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS): all participants who had been exposed to study drug irrespective of their compliance to the planned course of treatment. Participants not evaluable (NE) were due to patient withdraw, refusal, non-trial drug related AEs, and death

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as Assessed by an			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines [units: participants]			
Responders with CR	0	2	0
Responders with nPR	0	0	1
Responders with PR	47	46	9
Non-responders with SD	33	52	4
Non-responders with PD	5	9	1
NE	10	3	1

Statistical Analysis 1 for Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as Assessed by an Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines

Groups	2000 mg Ofatumumab + DR
Method	Other [Two-sided exact binomial test]
P-Value	<0.0001
Other Estimated Parameter [percentage of responders]	0.49
95.3% Confidence Interval	0.39 to 0.60

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

The p value is testing the hypothesis that the response rate is equal to 15% versus the response rate is not equal to 15%.

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

Two-sided 95.3% exact confidence intervals were calculated based on the binomial distribution.

Statistical Analysis 2 for Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as Assessed by an Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines

Groups	2000 mg Ofatumumab + BFR
Method	Other [Two-sided exact binomial test]
P-Value	<0.0001
Other Estimated Parameter [percentage of responders]	0.43
95.3% Confidence Interval	0.33 to 0.53

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

The p value is testing the hypothesis that the response rate is equal to 15% versus the response rate is not equal to 15%.

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

Two sided 95.3% exact confidence intervals were calculated based on the binomial distribution.

Statistical Analysis 3 for Number of Participants (Par.) Classified as Responders and Non-responders for Objective Response as

Assessed by an Independent Endpoint Review Committee (IRC) in Accordance With the National Cancer Institute Working Group (NCIWG) 1996 Guidelines

Groups	2000 mg Ofatumumab + Other
Method	Other [Two-sided exact binomial test]
P-Value	<0.001
Other Estimated Parameter [percentage of responders]	0.63
95.3% Confidence Interval	0.35 to 0.85

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

The p value is testing the hypothesis that the response rate is equal to 15% versus the response rate is not equal to 15%.

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

Two-sided 95.3% exact confidence intervals were calculated based on the binomial distribution.

2. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	Duration of response is defined as the time from the initial response (first visit at which response is observed) to progression or death. If the participant had progression between scheduled visits, no progression at the end of the trial, treatment discontinuation for undocumented progression, treatment discontinuation for toxicity or other reason, new anti-cancer treatment, and experienced death or progression after two or more missed visits in a row the endpoint was censored.

Time Frame	Start of treatment (Week 0 of Visit 2) until Week 24
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Duration of Response [units: months] Median (95% Confidence Interval)	5.5 (3.7 to 7.2)	6.4 (4.6 to 7.0)	7.4 (2.8 to 12.4)

3. Secondary Outcome Measure:

Measure Title	Progression-Free Survival (PFS)
Measure Description	PFS is defined as the time from randomization until progression/death. Per the IRC, if the participant had progression between scheduled visits, died before the first assessment, or died between adequate visits, the endpoint was considered progressed. If there was no progression at the end of the trial, treatment discontinuation for undocumented progression, treatment discontinuation for toxicity/other reason, new anti-cancer treatment, and death/progression after 2 or more missed visits in a row, the endpoint was censored. Clinical progression is not considered as progression endpoint.
Time Frame	Start of treatment (Week 0 of Visit 2) until Week 24
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were

	Description
	refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Progression-Free Survival (PFS) [units: months] Median (95% Confidence Interval)	4.6 (3.9 to 6.3)	5.5 (4.6 to 6.4)	8.9 (3.7 to 11.8)

4. Secondary Outcome Measure:

Measure Title	Time to Next Chronic Lymphocytic Leukemia (CLL) Treatment
Measure Description	Time to next chronic lymphocytic leukemia (CLL) treatment is defined as the time from treatment allocation/randomization (Visit 2) until the time of the first administration of the next CLL treatment other than

	ofatumumab (or HuMaxCD20, a fully human monoclonal antibody to CD20 that is expressed on the surface of B-cells).
Time Frame	Time from randomization (Week 0 of Visit 2) until the time of first administration of a CLL treatment other than ofatumumab (assessed for a median of 8.7 weeks currently [or up to 13.3 months])
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Time to Next Chronic Lymphocytic Leukemia (CLL) Treatment [units: months] Median (95% Confidence Interval)	8.5 (7.2 to 9.9)	8.2 (7.0 to 9.3)	12.1 (8.2 to 14.7)

5. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	OS is defined as the time from allocation to death. OS will also be subgrouped for responders and non-responders.
Time Frame	Start of randomization (Week 0 of Visit 2) until death (up to a median of 17.1 weeks)
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven

	Description
	weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Overall Survival [units: months] Median (95% Confidence Interval)	13.9 (9.8 to 18.6)	17.4 (15.0 to 24.5)	28.3 (19.0 to 29.2)

6. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 7 in Peripheral CD5+CD19+ Cell Counts
Measure Description	The peripheral blood for each participant was collected and analyzed for CD5+CD19+ cell counts. CD is “cluster of differentiation,” is a cell surface marker for immunophenotyping, and, in this case, is a surrogate for B cell malignancy (indicates malignant B cells). Percent change from Visit 2 (Week 0, Baseline) = (value at Week 7 minus value at Week 0 divided by value at Week 0) x 100.

Time Frame	Baseline (Visit 2) until Week 7 (Visit 9)
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Percent Change From Baseline to Week 7 in Peripheral CD5+CD19+ Cell Counts [units: percent change in cell counts] Median (Full Range)	-93 (-100 to 597)	-92 (-100 to 1384)	-95 (-100 to 640)

7. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 7 in Peripheral CD5+CD20+ Cell Counts
Measure Description	The peripheral blood for each participant was collected and analyzed for CD5+CD20+ cell counts. CD is “cluster of differentiation,” is a cell surface marker for immunophenotyping, and, in this case, is a surrogate for B cell malignancy (indicates malignant B cells). Percent change from Visit 2 (Week 0, Baseline) = (value at Week 7 minus value at Week 0 divided by value at Week 0) x 100.
Time Frame	Baseline (Visit 2) until Week 7 (Visit 9)
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were

	Description
	refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Percent Change From Baseline to Week 7 in Peripheral CD5+CD20+ Cell Counts [units: percent change in cell counts] Median (Full Range)	-100 (-100 to 236)	-100 (-100 to -13)	-100 (-100 to -96)

8. Secondary Outcome Measure:

Measure Title	Median Percent Change of Tumor Size (Sum of Products Dimensions [SPD]) From Baseline (Visit 2) to Week 24 (Visit 14)

Measure Description	Tumor size and change in tumor size will be measured by the absolute value of and the percent change in the sum of products of the diameters of the largest abnormal lymph nodes from Baseline to Week 24 (Visit 14). Percent change from Visit 2 (Baseline, Week 0) = (value at Week 24 minus value at Week 0 divided by value at Week 0) x 100.
Time Frame	Baseline (Visit 2) until Week 24 (Visit 14)
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Median Percent Change of Tumor Size (Sum of Products Dimensions [SPD]) From Baseline (Visit 2) to Week 24 (Visit 14) [units: percent change in tumor size] Median (Full Range)	-81 (-100 to 100)	-80 (-100 to 335)	-82 (-100 to -6)

9. Secondary Outcome Measure:

Measure Title	Number of Participants With Complete Resolution of Constitutional Symptoms at Week 24
Measure Description	Participants with complete resolution of constitutional symptoms were those in whom no constitutional symptoms, such as night sweats, weight loss, and fever or extreme fatigue, were observed.
Time Frame	Baseline (Visit 2) and Week 24
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants with constitutional symptoms at baseline attending each visit. Participants withdrawn during the study were not analyzed. (Participants without baseline constitutional symptoms did not experience new constitutional symptoms during the trial period.)

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg

	Description
	for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	42	57	10
Number of Participants With Complete Resolution of Constitutional Symptoms at Week 24 [units: participants]	34	46	9

10. Secondary Outcome Measure:

Measure Title	Number of Participants With Complete Resolution of Lymphadenopathy

Measure Description	Participants with complete resolution of lymphadenopathy (disease involving the lymph nodes) were defined as those in whom all observed lymph nodes were of normal size (all nodes <1 centimeters) as determined by physical examination assessed by the investigator. All palpable lymph node sizes were recorded.
Time Frame	Baseline (Visit 2) to end of study (up to Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants with lymphadenopathy at baseline attending each visit. Participants withdrawn during the study were not analyzed. (Participants without baseline lymphadenopathy remained free of lymphadenopathy during the trial.)

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	82	100	13
Number of Participants With Complete Resolution of Lymphadenopathy [units: participants]	27	18	6

11. Secondary Outcome Measure:

Measure Title	Number of Participants With Improvement on the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale at Week 24
Measure Description	ECOG performance status is a measure of the participant's ability to carry out activities of daily living on 6-point scale (0=fully active, 1=restricted in physically activity, ambulatory, 2=ambulatory [>50% of waking hours], 3=capable of only limited self care, 4=completely disabled, 5=Dead). Improvement in ECOG performance status is defined as a decrease from baseline by at least one score on the ECOG scale.
Time Frame	Baseline (Visit 2) and Week 24
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for participants (par.) with an ECOG score >0 at baseline attending each visit. Par. withdrawn from the study were not analyzed. (55 par. had an ECOG performance status of 0 at baseline and therefore did not have the opportunity to improve. No par. with an ECOG score of 0 at baseline worsened during the trial.)

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	55	70	12
Number of Participants With Improvement on the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale at Week 24 [units: participants]	25	35	7

12. Secondary Outcome Measure:

Measure Title	Number of Participants Who Were Positive, Negative, or Had Missing Data for the Indicated Fluorescence in Situ Hybridization (FISH) Prognostic Factors at Screening
Measure Description	The number of participants (par.) who were positive, negative, or had missing data for the following prognostic factors indicative of altered responsiveness to treatment and/or survival was measured: 17p-, 11q-, +12q, 6q-, 13q-. Par. were assessed by FISH for these chromosomal abnormalities known tobe prognostic for time to treatment and survival when detected at diagnosis. Par. were categorized by the chromosomal abnormality detected: 17 p deletion, 11q deletion (but not 17 p deletion), 12 q trisomy (but not 17 p or 111q deletion), 13q deletion only, and no chromosomal abnormalities found.
Time Frame	Screening (Visit 1, <=14 days prior to Visit 2)
Safety Issue?	No

Analysis Population Description

FAS. Par. were categorized hierarchically (by severity of abnormality): par. with a 17 p deletion (D); par. with an 11q D, but not a 17 p D; par. with 12q trisomy, but not a 17p or 11q D; par. with no aberrations found; par. with a 13q D as the sole aberration; and par. with 6q D (and not any of the above categories). Some par. had missing data.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as

	Description
	BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	92	110	16
Number of Participants Who Were Positive, Negative, or Had Missing Data for the Indicated Fluorescence in Situ Hybridization (FISH) Prognostic Factors at Screening [units: participants]			
FISH 17p-, negative	64	89	14
FISH 17p-, positive	27	19	1
FISH 17p-, missing	4	4	1
FISH 11q-, negative	56	69	11
FISH 11q-, positive	36	41	5
FISH 11q-, missing	3	2	0
FISH +12q, negative	76	91	11

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
FISH +12q, positive	15	19	5
FISH +12q, missing	4	2	0
FISH 6q-, negative	89	101	15
FISH 6q-, positive	2	9	0
FISH 6q-, missing	4	2	1
FISH 13q-, negative	46	53	9
FISH 13q-, positive	45	57	7
FISH 13q-, missing	4	2	0

13. Secondary Outcome Measure:

Measure Title	Number of Participants With Improvement in Hemoglobin
Measure Description	The number of participants (par.) who had improvement in hemoglobin levels >=11 grams (g)/deciliter (dl) (6.8 millimoles/liter) or 50% improvement over baseline was measured.
Time Frame	Baseline (Visit 2) to Week 28
Safety Issue?	No

Analysis Population Description

FAS. Par. were excluded from analysis if they received treatment of red blood cells (RBCs), received transfusions or a RBC growth factor (erythropoietin), died, withdrew from the trial, or began next CLL treatment. Only those par. remaining in the study at Week 28 were analyzed. No par. in the “Other” treatment arm met the criteria for analysis.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	49	62	8
Number of Participants With Improvement in Hemoglobin [units: participants]	18	20	5

14. Secondary Outcome Measure:

Measure Title	Number of Participants With Improvement in

	Thrombocytopenia (Thromb.)
Measure Description	Improvement in thromb. is defined as a decrease from Visit 2 by >=1 National Cancer Institute Common Terminology Criteria (NCI CTC) grade. Thromb. is defined as low platelet counts resulting from refractory CLL, damage from prior treatment, advanced age, or reduced bone marrow function and can be considered as an adverse condition. Adverse events (AEs) such as thromb. in a cancer indication are graded on a scale determined by the NCI called the NCI CTC: lowest, grade 1; highest, grade 5 (death). Changes in this grading can assess improvements or declines in the severity of the AE.
Time Frame	Baseline (Visit 2) to Week 28
Safety Issue?	No

Analysis Population Description

FAS. Only those participants remaining in the study at Week 28 were analyzed. No par. in the “Other” treatment arm met the criteria for analysis.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg

	Description
	for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	10	13	0
Number of Participants With Improvement in Thrombocytopenia (Thromb.) [units: participants]	4	6	

15. Secondary Outcome Measure:

Measure Title	Number of Participants With Complete Resolution of Hepatomegaly
Measure Description	Participants with complete resolution of enlarged liver (hepatomegaly) were defined as those with an enlarged palpable liver at baseline followed by the absence of hepatomegaly post- baseline (i.e., the liver was of normal size). Liver size was assessed by physical examination and documented as “centimeters” under the costal margin with relative changes in spleen size in 1 dimension calculated based on palpated numeric measurements (as per the 1996 NCIWG guidelines).
Time Frame	Baseline (Visit 2) until Week 24
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants with hepatomegaly from baseline attending each visit. Participants withdrawn during the study were not analyzed. Only participants with baseline hepatomegaly and a post-baseline assessment are included.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	21	28	7
Number of Participants With Complete Resolution of Hepatomegaly [units: participants]	17	19	4

16. Secondary Outcome Measure:

Measure Title	Number of Participants With Improvement in Neutropenia
Measure Description	Low levels of neutrophils (neutropenia) may increase the risk of developing serious infections and may be considered an adverse condition and evaluated on the NCI CTC with a grade. Improvement in neutropenia is defined as a decrease from Visit 2 (baseline) by at least one NCI CTC grade. Improvement is defined as a decrease from Visit 2 by at least one NCI CTC grade.
Time Frame	Baseline (Visit 2) to Week 28
Safety Issue?	No

Analysis Population Description

FAS. Only those par. remaining in the study at Week 28 were analyzed. No par. in the “Other” treatment arm met the criteria for analysis.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg

	Description
	for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	30	25	3
Number of Participants With Improvement in Neutropenia [units: participants]	20	17	1

17. Secondary Outcome Measure:

Measure Title	Number of Participants With Complete Resolution of Splenomegaly
Measure Description	Participants with complete resolution of enlarged spleen (splenomegaly) were defined as those with an enlarged palpable spleen at baseline followed by the absence of splenomegaly post-baseline (i.e., the spleen was of normal size). Spleen size was assessed by physical examination and documented as “centimeters” under the costal margin with relative changes in spleen size in 1 dimension calculated based on palpated numeric measurements (as per the 1996 NCIWG guidelines).
Time Frame	Baseline (Visit 2) until Week 24
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants with splenomegaly at baseline attending each visit. Participants withdrawn during the study were not analyzed. Only participants with baseline splenomegaly and a post-baseline assessment are included.

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	43	63	10
Number of Participants With Complete Resolution of Splenomegaly [units: participants]	28	38	5

18. Secondary Outcome Measure:

Measure Title	Number of Participants Who Experienced Any Adverse Event
Measure Description	An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which did not necessarily have a causal relationship with the treatment. A list of AEs experienced in the study with a frequency threshold of 5% can be found in the AE section of this results record.
Time Frame	From first infusion (Visit 2/Week 0) to Visit 21 (Month 24 of follow-up [up to Month 48]) or time of withdrawal (treatment and follow-up)
Safety Issue?	Yes

Analysis Population Description

FAS

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab +	Ofatumumab iv infusion was initiated at 300 mg, followed by seven

	Description
Other	weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Measured Values

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Number of Participants Analyzed	95	112	16
Number of Participants Who Experienced Any Adverse Event [units: participants]	90	107	16

19. Secondary Outcome Measure:

Measure Title	Cmax and Ctrough at Dose 1 (Visit 2, Week 0), Dose 8 (Visit 9, Week 7), and Dose 12 (Visit 14, Week 24)
Measure Description	Cmax is defined as the maximum concentration of drug in serum samples. Ctrough is defined as the trough serum concentration (measured concentration at the end of a dosing interval [taken directly before the next administration]). No drug was present before the first infusion; therefore, there are no Ctrough results for Dose 1
Time Frame	Visit 2 (Week 0), Visit 9 (Week 7), and Visit 14 (Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending each visit. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
2000 mg Ofatumumab + Total	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. Data from all three groups of participants (DR, BFR, and Other) have been combined.

Measured Values

	2000 mg Ofatumumab + Total
Number of Participants Analyzed	215
Cmax and Ctrough at Dose 1 (Visit 2, Week 0), Dose 8 (Visit 9, Week 7), and Dose 12 (Visit 14, Week 24) [units: Milligrams per liter (mg/L)] Geometric Mean (Geometric Coefficient of Variation)	
Cmax at Dose 1, n=215	61.4 (0.73%)
Ctrough at Dose 8, n=192	549 (2.34%)
Cmax at Dose 8, n=193	1391 (0.46%)
Ctrough at Dose 12, n=106	32.1 (58.8%)
Cmax at Dose 12, n=106	827 (0.41%)

20. Secondary Outcome Measure:

Measure Title	AUC (0-inf) and AUC(0-tau) at Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24)

Measure Description	AUC is defined as the area under the ofatumumab concentration-time curve as a measure of drug exposure. AUC(0-inf) is AUC from the start of infusion extrapolated to infinity. AUC(0-tau) is AUC from the start of infusion over the dosing interval.
Time Frame	Visit 9 (Week 7) and Visit 14 (Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending each visit for whom the parameter could be calculated. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
2000 mg Ofatumumab + Total	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. Data from all three groups of participants (DR, BFR, and Other) have been combined

Measured Values

	2000 mg Ofatumumab + Total
Number of Participants Analyzed	163
AUC (0-inf) and AUC(0-tau) at Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24) [units: Milligrams x hour per liter (mg.h/L)] Geometric Mean (Geometric Coefficient of Variation)	
AUC(0-inf) at Dose 8, n=133	463418 (0.94%)

	2000 mg Ofatumumab + Total
AUC(0-inf) at Dose 12, n=83	203536 (1.64%)
AUC(0-tau) at Dose 8, n=163	171286 (0.48%)
AUC(0-tau) at Dose 12, n=84	165617 (1.23%)

21. Secondary Outcome Measure:

Measure Title	Half-life (t1/2) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24)
Measure Description	Half-life (t1/2) is defined as the terminal half-life and is the time required for the amount of drug in the body to decrease by half.
Time Frame	Visit 9 (Week 7) and Visit14 (Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending each visit for whom the parameter could be calculated. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
2000 mg Ofatumumab + Total	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. Data from all three groups of participants (DR, BFR, and Other) have been combined.

Measured Values

	2000 mg Ofatumumab + Total
Number of Participants Analyzed	141
Half-life (t1/2) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24) [units: hours] Geometric Mean (Geometric Coefficient of Variation)	
t1/2 at Dose 8, n=141	326 (0.56%)
t1/2 at Dose 12, n=81	277 (0.87%)

22. Secondary Outcome Measure:

Measure Title	Clearance (CL) After Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24)
Measure Description	CL is the clearance of drug from serum, which is defined as the volume of serum from which the drug is cleared per unit time.
Time Frame	Visit 9 (Week 7) and Visit 14 (Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending each visit for whom the parameter could be calculated. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
2000 mg Ofatumumab + Total	Ofatumumab iv infusion was initiated at 300 mg, followed by seven

	Description
	weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. Data from all three groups of participants (DR, BFR, and Other) have been combined.

Measured Values

	2000 mg Ofatumumab + Total
Number of Participants Analyzed	163
Clearance (CL) After Dose 8 (Visit 9, Week 7) and Dose 12 (Visit 14, Week 24) [units: Milliliters per hour (mL/h)] Geometric Mean (Geometric Coefficient of Variation)	
CL at Dose 8, n=163	11.7 (0.48%)
CL at Dose 12, n=84	12.1 (1.23%)

23. Secondary Outcome Measure:

Measure Title	Volume of Distribution at Steady State (Vss) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24)
Measure Description	Vss is defined as the volume of distribution at steady state of ofatumumab.
Time Frame	Visit 9 (Week 7) and Visit 14 (Week 24)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending each visit for whom the parameter could be calculated. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
2000 mg Ofatumumab + Total	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. Data from all three groups of participants (DR, BFR, and Other) have been combined.

Measured Values

	2000 mg Ofatumumab + Total
Number of Participants Analyzed	133
Volume of Distribution at Steady State (Vss) at Dose 8 (Visit 9, Week 7) and at Dose 12 (Visit 14, Week 24) [units: Liters (L)] Geometric Mean (Geometric Coefficient of Variation)	
Vss at Dose 8, n=133	4.84 (0.30%)
Vss at Dose 12, n=83	3.73 (0.30%)

Reported Adverse Events

Reporting Groups

	Description
2000 mg Ofatumumab + DR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg

	Description
	for a duration of 24 weeks. The IRC classified these participants as DR, defined as participants who were enrolled in the study and were refractory to both fludarabine and alemtuzumab.
2000 mg Ofatumumab + BFR	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as BFR, defined as participants who were enrolled in the study and were refractory to fludarabine with bulky lymphadenopathy.
2000 mg Ofatumumab + Other	Ofatumumab iv infusion was initiated at 300 mg, followed by seven weekly 2000 mg infusions and then four monthly infusions of 2000 mg for a duration of 24 weeks. The IRC classified these participants as "other,"defined as participants who were enrolled in the study but did not meet criteria for DR or BFR.

Serious Adverse Events

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Total # participants affected/at risk	60/95 (63.16%)	59/112 (52.68%)	12/16 (75%)
Blood and lymphatic system disorders			
Agranulocytosis †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Anemia † [A]			
# participants affected/at risk	2/95 (2.11%)	1/112 (0.89%)	0/16 (0%)
# events			
Anemia haemolytic autoimmune † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Febrile neutropenia † [A]			
# participants affected/at risk	2/95 (2.11%)	3/112 (2.68%)	1/16 (6.25%)
# events			
Hemolytic anaemia † [A]			
# participants affected/at risk	0/95 (0%)	2/112 (1.79%)	0/16 (0%)
# events			
Lymphocytic infiltration † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Neutropenia † [A]			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# participants affected/at risk	7/95 (7.37%)	3/112 (2.68%)	3/16 (18.75%)
# events			
Thrombocytopenia † [A]			
# participants affected/at risk	4/95 (4.21%)	1/112 (0.89%)	0/16 (0%)
# events			
Cardiac disorders			
Cardiac arrest † [A]			
# participants affected/at risk	0/95 (0%)	2/112 (1.79%)	0/16 (0%)
# events			
Cardic failure † [A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
Myocardial infarction † [A]			
# participants affected/at risk	1/95 (1.05%)	2/112 (1.79%)	0/16 (0%)
# events			
Myocardial ischaemia † [A]			
# participants affected/at	0/95 (0%)	2/112 (1.79%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk			
# events			
Myopericarditis † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Ear and labyrinth disorders			
Vertigo † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Eye disorders			
Diplopia † [A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
Gastrointestinal disorders			
Abdominal pain † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Ascites †[A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
Constipation †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Diarrhea †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Enteritis †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Gastrointestinal pain †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Small intestinal obstruction			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
† [A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
General disorders			
Disease progression † [A]			
# participants affected/at risk	4/95 (4.21%)	5/112 (4.46%)	1/16 (6.25%)
# events			
Hyperthermia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Infusion related reaction † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Pyrexia † [A]			
# participants affected/at risk	6/95 (6.32%)	4/112 (3.57%)	0/16 (0%)
# events			
Immune system			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
disorders			
Contrast media allergy † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Cytokine release syndrome † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Hypersensitivity † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Immunodeficiency † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Infections and infestations			
Appendicitis † [A]			
# participants affected/at	0/95 (0%)	0/112 (0%)	1/16 (6.25%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk			
# events			
Aspergilloma † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Bronchitis † [A]			
# participants affected/at risk	2/95 (2.11%)	0/112 (0%)	0/16 (0%)
# events			
Bronchopneumonia † [A]			
# participants affected/at risk	2/95 (2.11%)	1/112 (0.89%)	0/16 (0%)
# events			
Cellulitis † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Ear infection † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Eczema infected †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Enterocolitis infection †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Enterocolitis infections †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Erysipelas †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Escherichia sepsis †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Eye infection staphylococcal †[A]			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Folliculitis † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Fusarium infection † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Gastroenteritis † [A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
Herpes zoster † [A]			
# participants affected/at risk	2/95 (2.11%)	1/112 (0.89%)	0/16 (0%)
# events			
Infection † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Influenza † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Injection site infection † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Lobar pneumonia † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Lower respiration infection † [A]			
# participants affected/at risk	0/95 (0%)	2/112 (1.79%)	0/16 (0%)
# events			
Lung infection † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Neutropenic sepsis † [A]			
# participants affected/at risk	4/95 (4.21%)	0/112 (0%)	1/16 (6.25%)
# events			
Nocardiosis † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Peritoneal infection † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Pneumocystis jiroveci pneumonia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Pneumonia † [A]			
# participants affected/at risk	12/95 (12.63%)	12/112 (10.71%)	2/16 (12.5%)
# events			
Pneumonia fungal † [A]			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Progessive multifocal † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Pseudomonas infection † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Pseuromonas infection † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Respiratory tract infection † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Sepsis † [A]			
# participants affected/at risk	5/95 (5.26%)	6/112 (5.36%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Septic shock † [A]			
# participants affected/at risk	3/95 (3.16%)	0/112 (0%)	0/16 (0%)
# events			
Sinusitis † [A]			
# participants affected/at risk	2/95 (2.11%)	2/112 (1.79%)	0/16 (0%)
# events			
Upper respiratory tract infection † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Urinary tract infection † [A]			
# participants affected/at risk	2/95 (2.11%)	2/112 (1.79%)	0/16 (0%)
# events			
Injury, poisoning and procedural complications			
Accidental overdose † [A]			
# participants affected/at	1/95 (1.05%)	0/112 (0%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk			
# events			
Fall † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Lower limb fracture † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Postoperative fever † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Spinal compression fracture † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Transfusion reaction † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Investigations			
Blood lactate dehydrogenase increased † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Blood uric acid increased † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Neutrophil count decreased † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Metabolism and nutrition disorders			
Diabetes † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Diabetes mellitus inadequate control † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Hypercalcaemia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Hypokalemia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Musculoskeletal and connective tissue disorders			
Arthralgia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Back pain † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Bone pain †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer †[A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Bowen's disease †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Breast cancer †[A]			
# participants affected/at risk	1/95 (1.05%)	1/112 (0.89%)	0/16 (0%)
# events			
Chronic lymphocytic			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
leukaemia transformation † [A]			
# participants affected/at risk	2/95 (2.11%)	0/112 (0%)	0/16 (0%)
# events			
Chronic lympocytic leukaemia † [A]			
# participants affected/at risk	1/95 (1.05%)	3/112 (2.68%)	0/16 (0%)
# events			
Colon cancer † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Hodgkins disease † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Mantle cell lymphoma † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Neoplasm † [A]			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Skin cancer † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Squamous cell carcinoma of the skin † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Tumor lysis syndrome † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Nervous system disorders			
Cerebral ischemia † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Epilepsy † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Facial paresis † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Hemiparesis † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Ischaemic stroke † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Transient ischaemic attack † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Psychiatric disorders			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Confusional state † [A]			
# participants affected/at risk	2/95 (2.11%)	0/112 (0%)	0/16 (0%)
# events			
Renal and urinary disorders			
Urinary retention † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Respiratory, thoracic and mediastinal disorders			
Acute repiratory failure † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Bronchospasm † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Dyspnea † [A]			
# participants affected/at	1/95 (1.05%)	0/112 (0%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk			
# events			
Haemoptysis † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Hypoxia † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Lung disorder † [A]			
# participants affected/at risk	0/95 (0%)	1/112 (0.89%)	0/16 (0%)
# events			
Lung infiltration † [A]			
# participants affected/at risk	0/95 (0%)	0/112 (0%)	1/16 (6.25%)
# events			
Pleural effusion † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	1/16 (6.25%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Pulmonary edema †[A]			
# participants affected/at risk	0/95 (0%)	2/112 (1.79%)	0/16 (0%)
# events			
Pulmonary embolism †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Respiratory failure †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Skin and subcutaneous tissue disorders			
Pyroderma gangrenosum †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			
Rash †[A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Vascular disorders			
Deep vein thrombosis † [A]			
# participants affected/at risk	1/95 (1.05%)	2/112 (1.79%)	0/16 (0%)
# events			
Haematoma † [A]			
# participants affected/at risk	1/95 (1.05%)	0/112 (0%)	0/16 (0%)
# events			

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Total # participants affected/at risk	90/95 (94.74%)	107/112 (95.54%)	16/16 (100%)
Blood and lymphatic system disorders			
Anemia † [A]			
# participants affected/at	17/95	20/112	2/16 (12.5%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk	(17.89%)	(17.86%)	
# events			
Neutropenia † [A]			
# participants affected/at risk	19/95 (20%)	13/112 (11.61%)	5/16 (31.25%)
# events			
Gastrointestinal disorders			
Abdominal pain † [A]			
# participants affected/at risk	5/95 (5.26%)	7/112 (6.25%)	1/16 (6.25%)
# events			
Diarrhoea † [A]			
# participants affected/at risk	16/95 (16.84%)	16/112 (14.29%)	5/16 (31.25%)
# events			
Nausea † [A]			
# participants affected/at risk	13/95 (13.68%)	15/112 (13.39%)	1/16 (6.25%)
# events			
Vomiting † [A]			
# participants affected/at	7/95 (7.37%)	7/112 (6.25%)	1/16 (6.25%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
risk			
# events			
General disorders			
Chills † [A]			
# participants affected/at risk	13/95 (13.68%)	13/112 (11.61%)	2/16 (12.5%)
# events			
Fatigue † [A]			
# participants affected/at risk	12/95 (12.63%)	22/112 (19.64%)	1/16 (6.25%)
# events			
Oedema peripheral † [A]			
# participants affected/at risk	9/95 (9.47%)	14/112 (12.5%)	1/16 (6.25%)
# events			
Pyrexia † [A]			
# participants affected/at risk	22/95 (23.16%)	18/112 (16.07%)	7/16 (43.75%)
# events			
Infections and infestations			
Bronchitis † [A]			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# participants affected/at risk	14/95 (14.74%)	12/112 (10.71%)	0/16 (0%)
# events			
Herpes zoster †[A]			
# participants affected/at risk	6/95 (6.32%)	6/112 (5.36%)	0/16 (0%)
# events			
Lower respiratory tract infections †[A]			
# participants affected/at risk	5/95 (5.26%)	6/112 (5.36%)	3/16 (18.75%)
# events			
Nasopharyngitis †[A]			
# participants affected/at risk	10/95 (10.53%)	10/112 (8.93%)	1/16 (6.25%)
# events			
Pneumonia †[A]			
# participants affected/at risk	15/95 (15.79%)	15/112 (13.39%)	4/16 (25%)
# events			
Sinusitis †[A]			
# participants affected/at risk	7/95 (7.37%)	7/112 (6.25%)	1/16 (6.25%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Upper respiratory tract infection † [A]			
# participants affected/at risk	4/95 (4.21%)	17/112 (15.18%)	2/16 (12.5%)
# events			
Urinary tract infection † [A]			
# participants affected/at risk	4/95 (4.21%)	8/112 (7.14%)	1/16 (6.25%)
# events			
Metabolism and nutrition disorders			
Decreased appetite † [A]			
# participants affected/at risk	8/95 (8.42%)	4/112 (3.57%)	0/16 (0%)
# events			
Musculoskeletal and connective tissue disorders			
Back pain † [A]			
# participants affected/at risk	13/95 (13.68%)	7/112 (6.25%)	2/16 (12.5%)

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
# events			
Muscle spasms † [A]			
# participants affected/at risk	4/95 (4.21%)	7/112 (6.25%)	2/16 (12.5%)
# events			
Nervous system disorders			
Headache † [A]			
# participants affected/at risk	8/95 (8.42%)	5/112 (4.46%)	1/16 (6.25%)
# events			
Parasthesia † [A]			
# participants affected/at risk	5/95 (5.26%)	5/112 (4.46%)	2/16 (12.5%)
# events			
Psychiatric disorders			
Insomnia † [A]			
# participants affected/at risk	7/95 (7.37%)	7/112 (6.25%)	1/16 (6.25%)
# events			
Respiratory, thoracic and mediastinal disorders			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Cough †[A]			
# participants affected/at risk	23/95 (24.21%)	24/112 (21.43%)	5/16 (31.25%)
# events			
Dyspnoea †[A]			
# participants affected/at risk	19/95 (20%)	12/112 (10.71%)	3/16 (18.75%)
# events			
Skin and subcutaneous tissue disorders			
Hyperhidrosis †[A]			
# participants affected/at risk	6/95 (6.32%)	8/112 (7.14%)	1/16 (6.25%)
# events			
Rash †[A]			
# participants affected/at risk	17/95 (17.89%)	8/112 (7.14%)	5/16 (31.25%)
# events			
Urticaria †[A]			
# participants affected/at risk	5/95 (5.26%)	9/112 (8.04%)	2/16 (12.5%)
# events			

	2000 mg Ofatumumab + DR	2000 mg Ofatumumab + BFR	2000 mg Ofatumumab + Other
Vascular disorders			
Hypotension †[A]			
# participants affected/at risk	7/95 (7.37%)	6/112 (5.36%)	1/16 (6.25%)
# events			

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

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