ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 12/19/2013

ClinicalTrials.gov ID: NCT00410163

Study Identification

Unique Protocol ID:	111774
Brief Title:	Ofatumumab With Fludarabine and Cyclophosphamide in B-CLL Patients (BIFROST)
Official Title:	An Open-labeled, Randomized, Two-dose, Parallel Group Trial of Ofatumumab, a Fully Human Monoclonal Anti-CD20 Antibody, in Combination With Fludarabine and Cyclophosphamide, in Patients With Previously Untreated B-cell CLL
Secondary IDs:	Hx-CD20-407 [Genmab] The BIFROST trial

Study Status

Record Verification:	November 2013
Overall Status:	Completed
Study Start:	January 2007
Primary Completion:	March 2009 [Actual]
Study Completion:	May 2013 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? No Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 11719 Serial Number: 063 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	To investigate the safety and efficacy of two dose regimes of ofatumumab in combination with chemotherapy in previously untreated patients with B-CLL
Detailed Description:	

Conditions

Conditions:	Leukaemia, Lymphocytic, Chronic
Keywords:	B-cell cyclophosphamide fludarabine Chronic Lymphocytic Leukemia Ofatumumab

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2

Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	61 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Active Comparator 1 Each patient will receive a total of 6 infusions with ofatumumab every 4 weeks in combination with fludarabine and cyclophosphamide. The first infusion will be 300mg followed by 5 infusions of 500mg	Drug: Ofatumumab 500mg Ofatumumab 500mg or should be diluted into 1000mL pyrogenefree saline and administered as an IV infusion.Duration of infusion will be approximately 6½ hours.Infusions should be given every 4 weeks until a total of 6 infusions has been given. Drug: Fludarabine Fludarabine (25 mg/m2) should be administered as an IV infusion daily, Days 2 through 4 of Course 1, and Days 1 through 3 of Courses 2 through 6, every 4 weeks for 6 courses Drug: Cyclophosphamide Cyclophosphamide (250 mg/m2) should be administered as an IV infusion daily, Days 2 through 4 of Course 1, and Days 1 through 3 of Courses 2 through 6, every 4 weeks for 6 courses.
Active Comparator: Active Comparator 2 Each patient will receive a total of 6 monthly infusions with ofatumumab in combination with fludarabine and cyclophosphamide. The first infusion will be 300mg followed by 5 infusions of 1000mg	Drug: Ofatumumab 1000mg Ofatumumab 1000mg or should be diluted into 1000mL pyrogenefree saline and administered as an IV infusion.Duration of infusion will be approximately 6½ hours.Infusions should be given every 4 weeks until a total of 6 infusions has been given. Drug: Fludarabine Fludarabine (25 mg/m2) should be administered as an IV infusion daily, Days 2 through 4 of Course 1, and Days 1 through 3 of Courses 2 through 6, every 4 weeks for 6 courses Drug: Cyclophosphamide Cyclophosphamide (250 mg/m2) should be administered as an IV infusion daily, Days 2 through 4 of Course 1, and Days 1 through 3 of Courses 2 through 6, every 4 weeks for 6 courses.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

1. Patients with active B-CLL and with an indication for treatment
2. Age ≥ 18 years
3. Following receipt of verbal and written information about the study, the patient must provide signed informed consent before any study related activity is carried out

Exclusion Criteria:

1. Any previous treatment for B-CLL or any other treatments that can be considered active against B-CLL
2. Glucocorticoid unless given in doses ≤ 10 mg /day for other indications than B-CLL (e.g. asthma)
3. Known transformation of B-CLL
4. Known CNS involvement of B-CLL
5. Past or current malignancy, except for:
    a. Cervical carcinoma Stage 1B or less
    b. Non-invasive basal cell and squamous cell skin carcinoma
    c. Malignant melanoma with a complete response of a duration of > 10 years
    d. Other cancer diagnoses with a complete response of a duration of > 5 years
6. Chronic or current infectious disease requiring systemic treatment
7. Clinically significant cardiac disease
8. Significant concurrent, uncontrolled medical condition
9. History of significant cerebrovascular disease
10. Known HIV positive
11. Positive serology for hepatitis B, unless due to vaccination
12. Leukapheresis, except as a safety measure before chemotherapy
13. ECOG Performance Status of 3 or 4
14. Patients who at the time of inclusion are not expected to be able to complete the ofatumumab-FC regimen
15. Patients who have received treatment with any non-marketed drug substance or experimental therapy within 4 weeks prior to Visit 1
16. Current participation in any other interventional clinical study
17. Patients known or suspected of not being able to comply with a study protocol (e.g. due to alcoholism, drug dependency or psychological disorder)
18. Breast feeding women or women with a positive pregnancy test at Visit 1
19. Women of childbearing potential not willing to use adequate contraception for up to one year after last dose of ofatumumab. Adequate contraception is defined as hormonal birth control or intrauterine device. For patients in the USA the use of a double barrier method is also considered adequate.

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations: United Kingdom
GSK Investigational Site
Plymouth, Devon, United Kingdom, PL68DH

United States, Texas
GSK Investigational Site
Houston, Texas, United States, 77030

References

Citations: Wierda WG, Kipps TJ, Durig J, Griskevicius L, Stilgenbauer S, Mayer J, et.al, Chemoimmunotherapy with O-FC in previously untreated patients with chronic lymphocytic leukemia. Blood 2011 June 16; 117: 6450-6458

Wierda WG, Kipps TJ, Dürig J, Griskevicius L, Stilgenbauer S, Mayer J et al.. Chemoimmunotherapy with Ofatumumab, Fludarabine and Cyclophosphamide (O-FC) in Previously Untreated Patients with Chronic Lymphocytic Leukemia (CLL). [Blood]. 2010;E pub ahead of print:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Participants received up to 6 courses (22 weeks) of treatment. After treatment, participants were evaluated for up to 18 months in a follow-up (FU) period and then entered an extended FU phase (up to Month 60). The overall study period reported is from 09 January 2007 to 05 June 2013, when all phases of the study were completed.

Reporting Groups

	Description
Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses. After the last infusion, the disease status of the participants was evaluated every 3 months up to 18 months during the Follow-up Period. Participants were monitored in the Extended Follow-up Phase every 6 months for survival until alternative Chronic Lymphocyte Leukemia (CLL) therapy was initiated, or until Month 60.
Ofatumumab 1000 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses. After the last infusion, the disease status of the participants was evaluated every 3 months up to 18 months during the Follow-up Period. Participants were monitored in the Extended Follow-up Phase every 6 months for survival until alternative CLL therapy was initiated, or until Month 60.

Treatment and Follow-up Phase (2 Years)

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC
Started	31	30
Completed	19	19
Not Completed	12	11
Adverse Event	4	2
Death	1	1
Withdrawal by Subject	2	1
Lack of Efficacy	0	4
Participant Had No Response	2	1
Participant Had Stable Disease	1	0
Participant Received New Therapy	1	1
Participant Had Bone Marrow Transplant	1	0
Investigator Decision	0	1

Extended Follow-up (FU) Phase (2-5 Years

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC
Started	20 [1]	21 [1]
Completed	10	11
Not Completed	10	10
Lost to Follow-up	3	1
Death	1	1
Medical Reasons	1	0
New Anti-CLL Treatment	4	8
Secondary Acute Myeloid Leukemia	1	0

[1] Participants who withdrew from the Treatment Phase were eligible to enter the Extended FU Phase.

Baseline Characteristics

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Baseline Measures

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC	Total
Number of Participants	31	30	61
Age, Continuous [units: Years] Mean (Standard Deviation)	56.1 (8.4)	56.4 (8.7)	56.2 (8.5)
Gender, Male/Female [units: Participants]			
Female	11	7	18

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC	Total
Male	20	23	43
Race/Ethnicity, Customized [units: participants]			
White	31	29	60
Black or African American	0	1	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants (Par.) With Complete Remission (CR), Measured From Start of Treatment Until 3 Months After Last Infusion
Measure Description	Par. were evaluated for response by an Independent Endpoint Review Committee (IRC) in accordance with the National Cancer Institute-sponsored Working Group (NCI-WG) 1996 guideline. Par. with Complete Remission (CR) were classified as "complete responders". As per NCI-WG, CR requires all of the following criteria for a period of >=2 months: absence of lymphadenopathy (all lymph nodes <1.0 centimeters), no hepatomegaly/splenomegaly, absence of constitutional symptoms, lymphocytes <=4.0*10^9/liter (L), neutrophil leukocytes >=1.5*10^9/L, platelets >100*10^9/L, and hemoglobin >11 grams/deciliter.
Time Frame	Start of treatment (Day 1 of Week 0) until 3 months after start of last infusion (up to Week 32)
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

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants (Par.) With Complete Remission (CR), Measured From Start of Treatment Until 3 Months After Last Infusion [units: participants]	10	15

2. Primary Outcome Measure:

Measure Title	Number of Participants (Par.) Who Were Classified as Responders and Non-responders
Measure Description	Par. were evaluated by an IRC in accordance with NCI-WG 1996 guideline. Responders: CR, Nodular Partial Remission (nPR, same as CR, but persistent bone marrow nodules), and Partial Remission (PR, >=50% decrease in lymphocytes from pretreatment baseline (BL) value, >=50% reduction in lymphadenopathy, >=50% reduction of liver/ spleen and neutrophils >= 1.5*10^9/L or platelets >100*10^9/L or hemoglobin >11 g/dL (or 50% improvement over BL for neutrophils, platelets, hemoglobin); non-responders: Stable Disease (SD, did not achieve CR/PR, and no PD), Progressive Disease (PD), or Not Evaluable (NE).
Time Frame	From start of treatment (Day 1 of Week 0) until 3 months after start of last infusion (up to Week 32)
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Number of Participants (Par.) Who Were Classified as Responders and Non-responders [units: participants]		

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
All responders	24	22
Responders, CR	10	15
Responders, nPR	1	1
Responders, PR	13	6
All Non-responders	7	8
Non-responders, SD	3	2
Non-responders, PD	2	5
Non-responders, NE	2	1

3. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	The duration of response was defined as the time from the initial response (the first visit at which response was observed) to progression or death. For participants who were lost to follow-up, duration of response was censored at the date of the last attended visit at which the endpoint was assessed.
Time Frame	From time of initial response to disease progression or death, whichever came first, assessed over 2 years
Safety Issue?	No

Analysis Population Description

FAS. Only those participants classified as responders were analyzed.

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	24	22
Duration of Response [units: months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] An insufficient number of participants experienced progression or death after response to reach a median or calculate a confidence interval.

4. Secondary Outcome Measure:

Measure Title	Progression-Free Survival
Measure Description	Progression-free survival (PFS) was defined as the time from randomization until the first radiologically or clinically documented evidence of progression or death due to any cause, if sooner. For participants who were lost to follow-up, PFS was censored at the date of the last attended visit at which the endpoint was assessed. The Kaplan-Meier method was used to estimate PFS.
Time Frame	From time of randomization to first documented evidence of disease progression or death due to any cause, whichever came first, assessed over 2 years
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Progression-Free Survival [units: months]	NA (NA to NA) [1]	23.5 (NA to NA) [2]

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Median (95% Confidence Interval)		

[1] An insufficient number of participants experienced progression or death to reach a median or calculate a confidence interval.
[2] An insufficient number of participants experienced progression or death to calculate a confidence interval.

5. Secondary Outcome Measure:

Measure Title	Time to Next Anti-chronic Lymphocytic Leukemia (CLL) Therapy or Death
Measure Description	Time to next anti-CLL (anti-lymphoma) therapy was defined as the time from randomization until the time of first administration of the next anti-lymphoma therapy other than ofatumumab or death. For participants who were lost to follow-up, the time was censored at the date of the last attended visit at which the endpoint was assessed.
Time Frame	From time of randomization to first administration of next anti-CLL therapy other than ofatumumab or death, assessed over 5 years
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Time to Next Anti-chronic Lymphocytic Leukemia (CLL) Therapy or Death [units: months] Median (95% Confidence Interval)	33.4 (27.3 to 46.9)	33.3 (26.7 to 54.6)

6. Secondary Outcome Measure:

Measure Title	Median Percent Change in Tumor Size From Baseline (Visit 2, Wk 0) at Visits 9, 21, 25, 29, 33, 34, 35, and 37
Measure Description	Tumor size was measured by physical examination of palpable abnormal lymph nodes. Percent change from Baseline (Visit 2, Week 0) = (value at indicated visits minus value at Visit 2 divided by value at Visit 2) * 100. Visits 33, 34, 35, 36, and 37 are measured in the number of months from the start of the last infusion. The start of the last infusion could have occurred up to Week 20.
Time Frame	Baseline Visit 2 (Week [Wk] 0); Visits 9 (Wk 4), 21 (Wk 12), 25 (Wk 16), 29 (Wk 20), 33 (Month [M] 1 after start of last infusion [LI]), 34 (M 3 after start of LI), 35 (M 6 after start of LI), 36 (M 9 after start of LI), and 37 (M 12 after start of L
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	29	28
Median Percent Change in Tumor Size From Baseline (Visit 2, Wk 0) at Visits 9, 21, 25, 29, 33, 34, 35, and 37 [units: percent change in tumor size] Median (Full Range)		
Visit 9 (Week 4), n=29, 28	-75.00 (-100.00 to 0.00)	-70.90 (-100.00 to 73.00)
Visit 21 (Week 12), n=24, 23	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to -39.00)
Visit 25 (Week 16), n=23, 20	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to -85.00)
Visit 29 (Week 20), n=22, 16	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to -92.00)
Visit 33 (Month 1), n=21, 24	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to -4.00)

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Visit 34 (Month 3), n=22, 23	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to -40.00)
Visit 35 (Month 6), n=19, 22	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to 12.00)
Visit 36 (Month 9), n=20, 22	-100.00 (-100.00 to 0.00)	-100.00 (-100.00 to 28.00)
Visit 37 (Month 12), n=20, 18	-100.00 (-100.00 to -100.00)	-100.00 (-100.00 to -69.00)

7. Secondary Outcome Measure:

Measure Title	Median Percent Change in CD5+CD19+ and CD5+CD20+ Cells in Peripheral Blood From Onset of Course 3 Throughout Follow-up (FU) Compared to Screening
Measure Description	Malignant B cells (CD5+CD19+ and CD5+CD20+) were measured in peripheral blood samples by flow cytometry. Percent change from Screening (Visit 1, Week -2) = (value at indicated visits minus value at Visit 1 divided by value at Visit 1) * 100. Visits 33 and 34 are measured in the number of months from the start of the last infusion. The start of the last infusion could have occurred up to Week 20.
Time Frame	Baseline Visit 2 (Week [Wk] 0); Visits 15 (Wk 8), 21 (Wk 12), 25 (Wk 16), 29 (Wk 20), 33 (Month [M] 1 after start of last infusion [LI]), 34 (M 3 after start of LI)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	25	26

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Median Percent Change in CD5+CD19+ and CD5+CD20+ Cells in Peripheral Blood From Onset of Course 3 Throughout Follow-up (FU) Compared to Screening [units: percent change in cells] Median (Full Range)		
CD5+CD19+ cells, Visit 15 (Wk 8), n=25, 26	-100.00 (-100.0 to 22.0)	-100.00 (-100.00 to -81)
CD5+CD19+ cells, Visit 21 (Wk 12), n=24, 24	-100.00 (-100.00 to -84.00)	-100.00 (-100.00 to -90.00)
CD5+CD19+ cells, Visit 25 (Wk16), n=23, 21	-100.00 (-100.00 to -93.00)	-100.00 (-100.00 to -96)
CD5+CD19+ cells, Visit 29 (Wk 20), n=22, 19	-100.00 (-100.00 to -98)	-100.00 (-100.00 to -96)
CD5+CD19+ cells, Visit 33 (Wk 24), n=21, 24	-100.00 (-100.00 to -99.00)	-100.00 (-100.00 to -73)
CD5+CD19+ cells, Visit 34 (Wk 32), n=20, 22	-100.00 (-100.00 to -95)	-100.00 (-100.00 to -97)
CD5+CD20+ cells, Visit 15 (Wk 8), n=25, 26	-100.00 (-100.00 to 22.00)	-100.00 (-100.00 to -92)
CD5+CD20+ cells, Visit 21 (Wk 12), n=24, 24	-100.00 (-100.00 to -84)	-100.00 (-100.00 to -96)
CD5+CD20+ cells, Visit 25 (Wk16), n=23, 21	-100.00 (-100.00 to -93)	-100.00 (-100.00 to -100)
CD5+CD20+ cells, Visit 29 (Wk 20), n=22, 19	-100.00 (-100.00 to -99)	-100.00 (-100.00 to -100)
CD5+CD20+ cells, Visit 33 (Wk 24), n=21, 24	-100.00 (-100.00 to -99)	-100.00 (-100.00 to -97.00)
CD5+CD20+ cells, Visit 34 (Wk 32), n=20, 22	-100.00 (-100.00 to -96)	-100.00 (-100.00 to -97.0)

8. Secondary Outcome Measure:

Measure Title	Number of Participants Who Experienced Any Adverse Event From First Treatment (Visit 2) to Visit 43 (Month 60)
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 this treatment. A list of AEs experienced in the study at a frequency threshold of 5% can be found in the AE section.
Time Frame	From first treatment (Visit 2) up to Visit 43 (Month 60)
Safety Issue?	Yes

Analysis Population Description

FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Number of Participants Who Experienced Any Adverse Event From First Treatment (Visit 2) to Visit 43 (Month 60) [units: participants]	31	30

9. Secondary Outcome Measure:

Measure Title	Number of Participants With Positive Human Anti-human Anti Bodies (HAHA) at Visits 1, 21, 35, and 39
Measure Description	HAHA are indicators of immunogenicity to ofatumumab. Blood samples were drawn from participants at Visits 1, 21, 35, and 39 for analysis of HAHA. Analysis of HAHA was done in batches.
Time Frame	Visits 1 (Screening, Visit -2), 21 (Week 12), 35 (Month 6), and 39 (Month 18)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Number of Participants With Positive Human Anti-human Anti Bodies (HAHA) at Visits 1, 21, 35, and 39 [units: participants]		
Visit 1 (Week -2), n=31, 30	0	0
Visit 21 (Week 12), n=24, 24	0	0
Visit 35 (Month 6), n=19, 22	0	0
Visit 39 (Month 18), n=14, 13	0	0

10. Secondary Outcome Measure:

Measure Title	Number of Participants Who Reported Myelosuppression (Anemia, Leukopenia, Neutropenia, and Thrombocytopenia)
Measure Description	Myelosuppression is one of the expected AEs for FC treatment and is defined as the decrease in the ability of the bone marrow to produce blood cells. The number of participants with myelosuppression was assessed from laboratory measurements with Grades 3(severe)-4 (life-threatening/disabling) (1, mild; 2, moderate; 5, death) according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0. The CTCAE is issued by the National Cancer Institute (NCI) and is the standard classification used for the severity grading scale for AEs in cancer therapy clinical studies.
Time Frame	From first treatment (Visit 2) up to Visit 43 (Month 60)
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Number of Participants Who Reported Myelosuppression (Anemia, Leukopenia, Neutropenia, and Thrombocytopenia) [units: participants]		
Anemia	6	8
Leukopenia	23	22
Neutropenia	29	26
Thrombocytopenia	4	8

11. Secondary Outcome Measure:

Measure Title	Percent Change From Screening (Visit 1) in Complement (CH50) Levels at Visit 9 (Week 4)
Measure Description	Blood samples were drawn from participants at Visits 1 and 9 for analysis of complement (CH50) levels. Analysis of CH50 was done in batches, and CH50 levels were measured two hours after the end of study medication infusion. Percent change from Screening (Visit 1, Week -2) = (value at Visit 9 minus value at Visit 1 divided by value at Visit 1) * 100.
Time Frame	Visit 1 (Week -2) and Visit 9 (Week 4)
Safety Issue?	No

Analysis Population Description

FAS. Data were provided for the number of participants attending Visit 9. Participants withdrawn during the study were not analyzed.

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	29	26
Percent Change From Screening (Visit 1) in Complement (CH50) Levels at Visit 9 (Week 4) [units: Percent change in complement levels] Median (Full Range)	0 (-54 to 520)	0 (-83 to 430)

12. Secondary Outcome Measure:

Measure Title	Number of Participants Classified as Responders Having CR Who Tested Negative for Minimal Residual Disease (MRD)
Measure Description	MRD refers to small number of leukemic cells that remain in the participant during treatment or after treatment when the participant has achieved CR. For all participants who achieved CR, the follow-up bone marrow sample was tested for malignant B cells (CD5+CD19+) to determine if there was any MRD.
Time Frame	From start of treatment (Day 1 of Week 0) until 3 months after start of last infusion (up to course 6 or Week 32)
Safety Issue?	No

Analysis Population Description

FAS. Only participants with CR at Visit 34 were analyzed.

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	10	15
Number of Participants Classified as Responders Having CR Who Tested Negative for Minimal Residual Disease (MRD)	2	6

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
[units: participants]		

13. Secondary Outcome Measure:

Measure Title	Ctrough and Cmax at the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20)
Measure Description	Cmax is defined as the maximum concentration of drug in plasma samples. Ctrough is defined as the trough plasma concentration (measured concentration at the end of a dosing interval [taken directly before next administration]). No drug is present before the first infusion; therefore, there are no Ctrough results for the first infusion.
Time Frame	Visit 2 (Week 0; up to 4 weeks after dose) and Visit 29 (Week 20; up to 9 months after dose)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	29
Ctrough and Cmax at the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20) [units: Milligrams per liter (mg/L)] Geometric Mean (Geometric Coefficient of Variation)		
First infusion, Cmax, n=31, 29	67.5 (0.47%)	57.2 (0.47%)
Sixth infusion, Cmax, n=22, 19	201 (0.30%)	427 (0.34%)
Sixth infusion, Ctrough, n=22, 19	19.9 (12.69%)	62.2 (10.36%)

14. Secondary Outcome Measure:

Measure Title	AUC(0-inf) and AUC(0-672) After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20)
Measure Description	AUC is defined as the area under the ofatumumab concentration-time curve as a measure of drug exposure. AUC(0-672) is AUC from start of infusion to 672 hours after start of infusion; AUC(0-inf) is AUC from start of infusion extrapolated to infinity.
Time Frame	Visit 2 (Week 0; up to 4 weeks after dose) and Visit 29 (Week 20; up to 9 months after dose)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	24	26
AUC(0-inf) and AUC(0-672) After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20) [units: Milligrams * hour per liter (mg.h/L)] Geometric Mean (Geometric Coefficient of Variation)		
First infusion, AUC(0-inf), n=24, 26	2453 (1.28%)	1915 (0.74%)
First infusion, AUC(0-672), n=24, 26	2452 (1.28%)	1915 (0.74%)
Sixth infusion, AUC(0-inf), n=16, 16	145236 (0.54%)	397577 (0.35%)
Sixth infusion, AUC(0-672), n=20, 19	74728 (0.39%)	149019 (0.75%)

15. Secondary Outcome Measure:

Measure Title	t1/2 After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20)
Measure Description	t1/2 is defined as terminal half-life and is the time required for the amount of drug in the body to decrease by half.
Time Frame	Visit 2 (Week 0; up to 4 weeks after dose) and Visit 29 (Week 20; up to 9 months after dose)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	24	26
t1/2 After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20) [units: hours] Geometric Mean (Geometric Coefficient of Variation)		
First infusion, t1/2, n=24, 26	19.4 (1.13%)	18.8 (0.62%)
Sixth infusion, t1/2, n=16, 16	551 (0.31%)	746 (0.30%)

16. Secondary Outcome Measure:

Measure Title	CL After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20)

Measure Description	CL is the clearance of drug from plasma, which is defined as the volume of plasma from which the drug is cleared per unit time.
Time Frame	Visit 2 (Week 0; up to 4 weeks after dose) and Visit 29 (Week 20; up to 9 months after dose)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	24	26
CL After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20) [units: Milliliters per hour (mL/h)] Geometric Mean (Geometric Coefficient of Variation)		
First infusion, CL, n=24, 26	122 (1.28%)	157 (0.74%)
Sixth infusion, CL, n=20, 19	6.7 (0.39%)	6.7 (0.75%)

17. Secondary Outcome Measure:

Measure Title	Vss After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20)
Measure Description	Vss is defined as the volume of distribution at steady state of ofatumumab.
Time Frame	Visit 2 (Week 0; up to 4 weeks after dose) and Visit 29 (Week 20; up to 9 months after dose)
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
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	24	26
Vss After the First Infusion (Visit 2, Week 0) and Sixth Infusion (Visit 29, Week 20) [units: liters] Geometric Mean (Geometric Coefficient of Variation)		
First infusion, Vss, n=24, 26	3.88 (0.37%)	4.57 (0.30%)
Sixth infusion, Vss, n=16, 16	5.15 (0.27%)	5.77 (0.38%)

18. Secondary Outcome Measure:

Measure Title	Number of Participants With Progression or Death
Measure Description	Disease progression is characterized by at least one of the following, per the Guidelines for the Diagnosis and Treatment of Chronic Lymphocytic Leukemia: a >=50% increase in the sum of the products of at least two lymph nodes on two consecutive determinations 2 weeks apart (at least one node must be >=2 centimeters); or the appearance of new palpable lymph nodes; or a >=50% increase in liver and/or spleen size (measurement below the costal margin); or the appearance of palpable hepatomegaly or splenomegaly not previously present; or a >=50% increase in the numbers of circulating lymphocytes to at least 5.0 * 10^9/Liter; or transformation to a more aggressive histology (e.g., Richter's syndrome or prolymphocytic leukemia with >55% prolymphocytes). For participants who were lost to follow-up, PFS was censored at the date of the last attended visit at which the endpoint was assessed. The Kaplan-Meier method was used to estimate PFS.
Time Frame	From time of randomization to first documented evidence of disease progression or death due to any cause, whichever came first, assessed over 2 years

Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Ofatumumab 500 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

Measured Values

	Ofatumumab 500 mg + FC	Ofatumumab 1000 mg + FC
Number of Participants Analyzed	31	30
Number of Participants With Progression or Death [units: Participants]	3	7

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	During the Extended Follow-up Phase, from 2 years to 5 years after first treatment, only serious adverse events (SAEs) were collected; no non-serious AEs were collected during this period.

Reporting Groups

	Description
Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab intravenous (iv) infusion initiated at 300 milligrams (mg) for course 1, followed by dose of 500 mg for courses 2-6 in combination with fludarabine iv (25 mg/meters squared [m^2] daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses
Ofatumumab 1000 mg + FC	Ofatumumab iv infusion initiated at 300 mg for course 1, followed by dose of 1000 mg for courses 2-6 in combination with fludarabine iv (25 mg/m^2 daily on Days 1-3) and cyclophosphamide iv (250 mg/m^2 daily on Days 1-3) administered every 4 weeks for a total of 6 courses

	Description
Ofatumumab 500 mg + FC: Extended Follow-up Phase	Participants were monitored in the Extended Follow-up Phase every 6 months for survival until alternative Chronic Lymphocyte Leukemia (CLL) therapy was initiated, or until Month 60.
Ofatumumab 1000 mg + FC: Extended Follow-up Phase	Participants were monitored in the Extended Follow-up Phase every 6 months for survival until alternative CLL therapy was initiated, or until Month 60.

Serious Adverse Events

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	17/31 (54.84%)	23/30 (76.67%)	7/31 (22.58%)	5/30 (16.67%)
Blood and lymphatic system disorders				
Anaemia [A] †	1/31 (3.23%)	1/30 (3.33%)	0/31 (0%)	1/30 (3.33%)
Anaemia haemolytic autoimmune [A] †	1/31 (3.23%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Febrile neutropenia [A] †	4/31 (12.9%)	3/30 (10%)	0/31 (0%)	0/30 (0%)
Leukopenia [A] †	3/31 (9.68%)	7/30 (23.33%)	0/31 (0%)	0/30 (0%)
Lymphopenia [A] †	0/31 (0%)	2/30 (6.67%)	0/31 (0%)	0/30 (0%)
Neutropenia [A] †	10/31 (32.26%)	16/30 (53.33%)	0/31 (0%)	1/30 (3.33%)
Thrombocytopenia [A] †	2/31 (6.45%)	3/30 (10%)	0/31 (0%)	0/30 (0%)
Cardiac disorders				
Cardiac failure congestive [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Myocardial infarction [A] †	2/31 (6.45%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Gastrointestinal disorders				
Aphthous stomatitis [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Mouth ulceration [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Nausea [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Subileus [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
General disorders				
Disease progression [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Oedema peripheral [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Pyrexia [A] †	3/31 (9.68%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Infections and infestations				
Acarodermatitis [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Bronchitis acute [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Eczema infected [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Gastroenteritis rotavirus [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Herpes virus infection [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Infection [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Laryngitis [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Pneumonia [A] †	2/31 (6.45%)	2/30 (6.67%)	0/31 (0%)	1/30 (3.33%)
Pneumonia fungal [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Progressive multifocal leukoencephalopathy [A] †	0/31 (0%)	0/30 (0%)	0/31 (0%)	1/30 (3.33%)
Respiratory tract infection [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Sepsis [A] †	0/31 (0%)	2/30 (6.67%)	0/31 (0%)	0/30 (0%)
Urinary tract infection [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Investigations				
Neutrophil count decreased [A] †	1/31 (3.23%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Metabolism and nutrition disorders				
Hyperglycaemia [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Musculoskeletal and connective tissue disorders				
Arthritis reactive [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Back pain [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Exostosis [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Rhabdomyolysis [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Acute myeloid leukemia [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Adenocarcinoma of colon [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Malignant melanoma [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Myelodysplastic syndrome [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Prostate cancer [A] †	0/31 (0%)	0/30 (0%)	0/31 (0%)	1/30 (3.33%)
Renal cell carcinoma stage unspecified [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Small cell lung cancer [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Nervous system disorders				
Cerebrovascular accident [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)
Psychiatric disorders				
Alcohol abuse [A] †	0/31 (0%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Depression [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)
Respiratory, thoracic and mediastinal disorders				
Bronchitis chronic [A] †	0/31 (0%)	0/30 (0%)	1/31 (3.23%)	0/30 (0%)

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dyspnoea [A] †	1/31 (3.23%)	1/30 (3.33%)	0/31 (0%)	0/30 (0%)
Vascular disorders				
Subclavian vein thrombosis [A] †	1/31 (3.23%)	0/30 (0%)	0/31 (0%)	0/30 (0%)

† 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%

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	31/31 (100%)	30/30 (100%)	0/0	0/0
Blood and lymphatic system disorders				
Anaemia [A] †	4/31 (12.9%)	5/30 (16.67%)	0/0	0/0
Febrile neutropenia [A] †	5/31 (16.13%)	5/30 (16.67%)	0/0	0/0
Leukopenia [A] †	8/31 (25.81%)	16/30 (53.33%)	0/0	0/0
Lymphopenia [A] †	5/31 (16.13%)	5/30 (16.67%)	0/0	0/0
Neutropenia [A] †	14/31 (45.16%)	23/30 (76.67%)	0/0	0/0
Thrombocytopenia [A] †	7/31 (22.58%)	12/30 (40%)	0/0	0/0
Ear and labyrinth disorders				
Vertigo [A] †	3/31 (9.68%)	1/30 (3.33%)	0/0	0/0
Gastrointestinal disorders				
Abdominal pain [A] †	1/31 (3.23%)	2/30 (6.67%)	0/0	0/0
Constipation [A] †	5/31 (16.13%)	5/30 (16.67%)	0/0	0/0

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Diarrhoea [A] †	5/31 (16.13%)	4/30 (13.33%)	0/0	0/0
Dispepsia [A] †	4/31 (12.9%)	0/30 (0%)	0/0	0/0
Nausea [A] †	14/31 (45.16%)	13/30 (43.33%)	0/0	0/0
Vomiting [A] †	9/31 (29.03%)	6/30 (20%)	0/0	0/0
General disorders				
Chills [A] †	4/31 (12.9%)	5/30 (16.67%)	0/0	0/0
Fatigue [A] †	8/31 (25.81%)	6/30 (20%)	0/0	0/0
Oedema [A] †	3/31 (9.68%)	2/30 (6.67%)	0/0	0/0
Oedema peripheral [A] †	4/31 (12.9%)	1/30 (3.33%)	0/0	0/0
Pyrexia [A] †	9/31 (29.03%)	7/30 (23.33%)	0/0	0/0
Infections and infestations				
Bronchitis [A] †	4/31 (12.9%)	2/30 (6.67%)	0/0	0/0
Herpes zoster [A] †	4/31 (12.9%)	1/30 (3.33%)	0/0	0/0
Nasopharyngitis [A] †	5/31 (16.13%)	4/30 (13.33%)	0/0	0/0
Pneumonia [A] †	2/31 (6.45%)	2/30 (6.67%)	0/0	0/0
Rhinitis [A] †	3/31 (9.68%)	2/30 (6.67%)	0/0	0/0
Sinusitis [A] †	4/31 (12.9%)	2/30 (6.67%)	0/0	0/0
Upper respiratory tract infections [A] †	4/31 (12.9%)	2/30 (6.67%)	0/0	0/0
Investigations				
Blood creatinine increased [A] †	1/31 (3.23%)	4/30 (13.33%)	0/0	0/0
Metabolism and nutrition disorders				

	Ofatumumab 500 mg + Fludarabine and Cyclophosphamide (FC)	Ofatumumab 1000 mg + FC	Ofatumumab 500 mg + FC: Extended Follow-up Phase	Ofatumumab 1000 mg + FC: Extended Follow-up Phase
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hyperkalaemia [A] †	2/31 (6.45%)	2/30 (6.67%)	0/0	0/0
Musculoskeletal and connective tissue disorders				
Arthralgia [A] †	5/31 (16.13%)	5/30 (16.67%)	0/0	0/0
Back pain [A] †	4/31 (12.9%)	1/30 (3.33%)	0/0	0/0
Joint swelling [A] †	3/31 (9.68%)	1/30 (3.33%)	0/0	0/0
Nervous system disorders				
Headache [A] †	7/31 (22.58%)	5/30 (16.67%)	0/0	0/0
Psychiatric disorders				
Insomnia [A] †	2/31 (6.45%)	4/30 (13.33%)	0/0	0/0
Respiratory, thoracic and mediastinal disorders				
Cough [A] †	4/31 (12.9%)	7/30 (23.33%)	0/0	0/0
Dyspnoea [A] †	4/31 (12.9%)	4/30 (13.33%)	0/0	0/0
Pharyngolaryngeal pain [A] †	2/31 (6.45%)	2/30 (6.67%)	0/0	0/0
Skin and subcutaneous tissue disorders				
Pruritus [A] †	3/31 (9.68%)	3/30 (10%)	0/0	0/0
Rash [A] †	10/31 (32.26%)	8/30 (26.67%)	0/0	0/0
Urticaria [A] †	6/31 (19.35%)	3/30 (10%)	0/0	0/0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

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.

Results Point of Contact:

Name/Official Title: GSK Response Center
Organization: GlaxoSmithKline
Phone: 866-435-7343
Email: