Clinical trial results:
A Phase II, Multi-centre Study Investigating the Safety and Efficacy of Ofatumumab and Bendamustine Combination in Patients with Untreated or Relapsed Chronic Lymphocytic Leukaemia (CLL)

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2011-005178-43
Trial protocol	CZ DE BE ES PL GR IT
Global end of trial date	25 November 2015

Results information

Result version number	v1 (current)
This version publication date	06 July 2018
First version publication date	06 July 2018

Trial information

Trial identification

Sponsor protocol code	115991/COMB157B2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01520922
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Pharma AG, CH-4002, Switzerland, Basel
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective: To evaluate the investigator-assessed overall response rate (ORR) in two study populations i.e., subjects with previously untreated chronic lymphocytic leukemia (CLL) and subjects with relapsed CLL who were administered ofatumumab and bendamustine.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	36 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	97
EEA total number of subjects	69

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	41
From 65 to 84 years	55
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants (par.) who met eligibility criteria at Screening were then allocated to one of the following populations: par. with previously untreated CLL or par. with relapsed CLL. A total of 99 par. were enrolled and 97 par. entered the treatment period. Study results do not include the 2 par. that were not treated in this study

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ofatumumab + Bendamustine 90 mg/m^2

Arm description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Arm title	Ofatumumab + Bendamustine 70 mg/m^2

Arm description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental

Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Number of subjects in period 1	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2
Started	44	53
Completed	39	45
Not completed	5	8
Physician decision	2	1
Adverse event, non-fatal	3	5
Progression	-	2

Period 2

Period 2 title	Follow up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ofatumumab + Bendamustine 90 mg/m^2

Arm description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Arm title	Ofatumumab + Bendamustine 70 mg/m^2

Arm description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Number of subjects in period 2	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2
Started	39	45
Completed	39	44
Not completed	0	1
Lost to follow-up	-	1

Period 3

Period 3 title	Survival follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ofatumumab + Bendamustine 90 mg/m^2

Arm description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Arm title	Ofatumumab + Bendamustine 70 mg/m^2

Arm description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Arm type	Experimental
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab is an immunoglobulin G1κ (IgG1κ) human monoclonal antibody that specifically recognises a distinct epitope encompassing both large and small extracellular loops on the human CD20 molecule expressed on B cells and binds to this site with high affinity with a dissociation half-life of approximately 3 hours. Ofatumumab induces more efficient complement-dependent cytotoxicity (CDC) mediated cell lysis in vitro, compared to rituximab, especially in low CD20 density cells

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Bendamustine is a cytostatic drug which structurally combines a purine-like benzamidazol nucleus and a bifunctional alkylating nitrogen mustard group. Bendamustine was provided to sites as single-use 25 mg (2.5 mg/mL) and 100 mg (2.5 mg/mL) vials of bendamustine HCl as lyophilized powder.

Number of subjects in period 3[1]	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2
Started	21	40
Completed	20	40
Not completed	1	0
Consent withdrawn by subject	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Data for survival follow up not available for entire cohort

Baseline characteristics

Reporting groups	
Reporting group title	Ofatumumab + Bendamustine 90 mg/m^2
Reporting group description:	
Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).	
Reporting group title	Ofatumumab + Bendamustine 70 mg/m^2
Reporting group description:	
Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).	

Reporting group values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2	Total
Number of subjects	44	53	97
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	63.2	66.5	
standard deviation	± 10.11	± 9.28	-
Gender categorical Units: Subjects			
Female	15	17	32
Male	29	36	65
RaceEthnicityOther Units: Subjects			
White - White/Caucasian/European Heritage	42	53	95
White - Arabic/North African Heritage	1	0	1
African American/African Heritage	1	0	1

End points

End points reporting groups

Reporting group title	Ofatumumab + Bendamustine 90 mg/m^2

Reporting group description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 70 mg/m^2

Reporting group description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 90 mg/m^2

Reporting group description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 70 mg/m^2

Reporting group description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 90 mg/m^2

Reporting group description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 70 mg/m^2

Reporting group description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Primary: Number of participants with overall response (OR), as assessed by the investigator

End point title	Number of participants with overall response (OR), as assessed by the investigator

End point description:

OR is defined as the number of participants achieving an objective response (complete response [CR], CR with incomplete bone marrow recovery [CRi], partial response [PR], and nodular PR [nPR]), after 3 cycles, after 6 cycles, and after the last dose of ofatumumab and bendamustine treatment. CR (all the criteria at least 2 months after last treatment): no lymphadenopathy (Ly)/ hepatomegaly/ splenomegaly/ constitutional symptoms; neutrophils >1500 per microliter (µL), platelets (PL) >100,000/µL, hemoglobin (Hb) >11 grams/deciliter (g/dL), lymphocytes (LC) <4000/µL, bone marrow (BM) sample must be normocellular for age, <30% LC, no lymphoid nodule. CRi: CR criteria, persistent anemia/thrombocytopenia/neutropenia unrelated to CLL but related to drug toxicity. PR: >=50% decrease in LC, Ly, size of liver and spleen and at least one of the following results: PL >100,000/µL or

50% improvement over Baseline (BL), Hb >11 g/dL or 50% improvement over BL, LC <4000/µL. nPR: persistent nodules BM.

End point type	Primary

End point timeframe:

From the start of study treatment until 3 months after the last dose of study treatment

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[1]	53[2]		
Units: Participants				
CR	19	6		
CRi	2	2		
nPR	4	8		
PR	17	23		

Notes:

[1] - As-treated subjects (ATS) Population

[2] - As-treated subjects (ATS) Population

Statistical analyses

Statistical analysis title	Investigator-assessed ORR: Untreated CLL
Comparison groups	Ofatumumab + Bendamustine 90 mg/m^2 v Ofatumumab + Bendamustine 70 mg/m^2
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percentage of participants
Point estimate	95
Confidence interval	
level	95 %
sides	2-sided
lower limit	84.53
upper limit	99.44

Statistical analysis title	Investigator-assessed ORR: Relapsed CLL
Comparison groups	Ofatumumab + Bendamustine 70 mg/m^2 v Ofatumumab + Bendamustine 90 mg/m^2
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage of participants
Point estimate	74

Confidence interval	
level	95 %
sides	2-sided
lower limit	59.67
upper limit	84.74

Secondary: Number of participants with overall response (OR) with Computed Tomography (CT) Scan (CT scan) assessment, as assessed by the investigator

End point title	Number of participants with overall response (OR) with Computed Tomography (CT) Scan (CT scan) assessment, as assessed by the investigator

End point description:

OR is defined as the number of participants achieving an objective response (complete response [CR], CR with incomplete bone marrow recovery [CRi], partial response [PR], and nodular PR [nPR]), after 3 cycles, after 6 cycles, and after the last dose of ofatumumab and bendamustine treatment. CR (all the criteria at least 2 months after last treatment): no lymphadenopathy (Ly)/ hepatomegaly/ splenomegaly/ constitutional symptoms; neutrophils >1500 per microliter (µL), platelets (PL) >100,000/µL, hemoglobin (Hb) >11 grams/deciliter (g/dL), lymphocytes (LC) <4000/µL, bone marrow (BM) sample must be normocellular for age, <30% LC, no lymphoid nodule. CRi: CR criteria, persistent anemia/thrombocytopenia/neutropenia unrelated to CLL but related to drug toxicity. PR: >=50% decrease in LC, Ly, size of liver and spleen and at least one of the following results: PL >100,000/µL or 50% improvement over Baseline (BL), Hb >11 g/dL or 50% improvement over BL, LC <4000/µL. nPR: persistent nodules BM.

End point type	Secondary

End point timeframe:

From the start of study treatment until 3 months after the last dose of study treatment

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[3]	53[4]		
Units: Participants				
CR	12	5		
CRi	1	2		
nPR	2	6		
PR	22	24		

Notes:

[3] - As-treated subjects (ATS) Population

[4] - As-treated subjects (ATS) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with complete response (CR) with and without a CT scan assessment after the last dose of study treatment, as assessed by the investigator

End point title	Number of participants with complete response (CR) with and without a CT scan assessment after the last dose of study treatment, as assessed by the investigator

End point description:

Response was determined according to the IWCLL updated NCI-WG guidelines 2008. CR requires all of the following criteria at least 2 months after the last treatment: no lymphadenopathy (Ly)/ hepatomegaly/ splenomegaly/ constitutional symptoms; neutrophils >1500/µL, platelets (PL) >100,000/µL, hemoglobin (Hb) >11.0 g/dL, lymphocytes (LC) <4000/µL, bone marrow (BM) sample must be normocellular for age, <30% LC, no lymphoid nodule.

End point type	Secondary

End point timeframe:

From the start of study treatment until 3 months after the last dose of study treatment

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[5]	53[6]		
Units: Participants				
CR without CT scan assessment	19	6		
CR with CT scan assessment	12	5		

Notes:

[5] - As-treated subjects (ATS) Population

[6] - As-treated subjects (ATS) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Kaplan-meier estimates of Time to response

End point title	Investigator-assessed Kaplan-meier estimates of Time to response

End point description:

Time to response is defined as time from date of the first administration of study treatment to the first response (CR, CRi, nPR, or PR). Response was determined according to the IWCLL updated NCI-WG guidelines 2008. CR: all of the following criteria at least 2 months after last treatment: no lymphadenopathy (Ly)/ hepatomegaly/ splenomegaly/ constitutional symptoms; neutrophils >1500 per microliter (µL), platelets (PL) >100,000/µL, hemoglobin (Hb) >11.0 grams/deciliter (g/dL), lymphocytes (LC) <4000/µL, bone marrow (BM) sample must be normocellular for age, <30% LC, no lymphoid nodule. CRi: CR criteria, persistent anemia/ thrombocytopenia/ neutropenia unrelated to CLL but related to drug toxicity. nPR: persistent nodules BM. PR: >=50% decrease in LC, Ly, size of liver and spleen and at least one of the following results: PL >100,000/µL or 50% improvement over Baseline (BL), Hb >11.0 g/dL or 50% improvement over BL, LC <4000/µL.

End point type	Secondary

End point timeframe:

From the start of study treatment to the first response (CR, CRi, nPR, or PR) (up to 3 Month Follow-up (F/U) visit)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[7]	47[8]		
Units: Months				
median (confidence interval 95%)	0.95 (0.95 to 1.02)	1.08 (0.95 to 1.87)		

Notes:

[7] - ATS Population. Only participants who had a response (CR, CRi, nPR, or PR) were evaluated.

[8] - ATS Population. Only participants who had a response (CR, CRi, nPR, or PR) were evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Kaplan-meier estimates of duration of response

End point title	Investigator-assessed Kaplan-meier estimates of duration of response

End point description:

The duration of response is defined as the time from the initial response (CR, CRi, nPR, or PR) to the first documented sign of disease progression (PD) or death due to any cause. PD requires at least one of the following: new lesion or increase by >=50% from Baseline in lymphocytes (LC) with at least 5000B-lymphocytes per microliter (5.0 x 10^9/L), lymphadenopathy (Ly), size of liver and spleen, platelets (PL) >= 50% decrease from Baseline, or to <100,000/uL secondary to CLL, hemoglobin (Hb) decrease of >2 g/dL from Baseline or to <10 g/dL secondary to CLL, CLL- transformation, cytopenia after treatment. Response was determined according to the IWCLL updated NCI-WG guidelines 2008.

End point type	Secondary

End point timeframe:

From time of initial response (CR, CRi, nPR, or PR) to disease progression or death, whichever came first (up to 3 years after the last doseof study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[9]	35		
Units: Months				
median (confidence interval 95%)	35.15 (33.05 to 37.13)	21.75 (14.75 to 26.41)		

Notes:

[9] - ATS Population only with an initial response with PD or death were assessed for duration of response

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed of Kaplan-meier estimates of Progression-free survival (PFS)

End point title	Investigator-assessed of Kaplan-meier estimates of Progression-free survival (PFS)

End point description:

PFS is defined as the interval of time between the date of the first administration of study treatment and

the earlier of the date of disease progression (PD) and the date of death due to any cause. PD requires at least one of the following:new lesion or increase by >=50% from BL in LC, Ly, size of liver and spleen, PL >= 50% decrease from BL, or to <100,000/uL secondary to CLL, Hb decrease of >2 g/dL from BL or to <10 g/dL secondary to CLL, CLL- transformation. Response was determined according to the IWCLL updated NCI-WG guidelines 2008. Participants who have neither progressed or died at the time of analysis were censored at the date of the last adequate assessment. If there was more than 1 scheduled visit missed, PFS is censored at the last adequate assessment of response. An adequate assessment is defined as an assessment where the investigator determined a response of CR, CRi, nPR, PR, or stable disease (SD).

End point type	Secondary

End point timeframe:

From the start of study treatment until earliest date of disease progression or death (up to 3 years after the last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[10]	39[11]		
Units: Months				
median (confidence interval 95%)	36.07 (34 to 38.05)	22.54 (14 to 27.33)		

Notes:

[10] - All Treated Subjects' (ATS) population. N= Progression or Death

[11] - All Treated Subjects' (ATS) population. N= Progression or Death

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Kaplan-meier estimates of Overall Survival

End point title	Investigator-assessed Kaplan-meier estimates of Overall Survival

End point description:

OS is defined as the interval of time between the date of the first administration of study treatment and the date of death due to any cause. For participants who did not die, time of death was censored at the date of last contact.

End point type	Secondary

End point timeframe:

From the start of study treatment to the date of death due to any cause (up to 3 years after the last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[12]	23[13]		
Units: Months				
median (confidence interval 95%)	99999.9 (-99999.9 to 999999.9)	99999.9 (-99999.9 to 999999.9)		

Notes:

[12] - Median was not available because over 50% of the all treated subjects were alive. N= Death

[13] - Median was not available because over 50% of the all treated subjects were alive. N= Death

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-Assessed Kaplan-Meier Estimates of Time to Progression

End point title	Investigator-Assessed Kaplan-Meier Estimates of Time to Progression

End point description:

Time to progression is defined as the time from the date of the first administration of study treatment to disease progression (PD). PD requires at least one of the following: new lesion or increase by >=50% from Baseline in lymphocytes (LC) with at least 5000 B-lymphocytes per microliter (5.0 x 10^9/L), lymphadenopathy (Ly), size of liver and spleen, platelets (PL) >= 50% decrease from Baseline, or to <100,000/uL secondary to CLL, hemoglobin (Hb) decrease of >2 g/dL from Baseline or to <10 g/dL secondary to CLL, CLL- transformation, cytopenia after treatment. Response was determined according to the IWCLL updated NCI-WG guidelines 2008.

End point type	Secondary

End point timeframe:

From the start of study treatment to disease progression (up to 3 years after the last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[14]	35[15]		
Units: Months				
median (confidence interval 95%)	36 (34 to 38.05)	22.67 (16.07 to 28.58)		

Notes:

[14] - All treated subjects (ATS). This analysis includes patients who had progression.

[15] - All treated subjects (ATS). This analysis includes patients who had progression.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to next therapy

End point title	Time to next therapy

End point description:

Time to next therapy is defined as the time from the date of the first administration of study treatment until the start of the next anti-CLL therapy.

End point type	Secondary

End point timeframe:

From the start of study treatment until the start of the next anti-CLL therapy (up to 3 years after the last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[16]	29[17]		
Units: Months				
median (confidence interval 95%)	31.18 (17.25 to 37.03)	16.82 (11.6 to 25.36)		

Notes:

[16] - ATS Population. Only participants that took anti-CLL therapy were evaluated.

[17] - ATS Population. Only participants that took anti-CLL therapy were evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is an event of possible drug-induced liver injury. Refer to the general Adverse AE/SAE module for a complete list of AEs and SAEs.

End point type	Secondary

End point timeframe:

From first dose of study medication to 60 days after the last dose of study medication (if the event is considered as an AE), or up to 3 years after the last dose of study treatment or until the time of the next anti-CLL therapy, if considered a SAE

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[18]	53[19]		
Units: Participants				
Any AE	43	50		
Any SAE	20	25		

Notes:

[18] - Safety Population: all participants who received at least one dose of ofatumumab or bendamustine

[19] - Safety Population: all participants who received at least one dose of ofatumumab or bendamustine

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Immunoglobulin (Ig) antibodies to End of study treatment

End point title	Change from Baseline in the Immunoglobulin (Ig) antibodies to End of study treatment

End point description:

Immunoglobulins, or antibodies, are large proteins used by the immune system to identify and neutralize foreign particles such as bacteria and viruses. Their normal blood levels indicate proper immune status. Low levels indicate immuno-suppression. IgA, IgG, and IgM were measured in the blood samples of the participants. Baseline IgA, IgG, and IgM values are the last pre-dose assessment values performed on cycle 1 Day 1. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and end of study treatment (up to 30 months)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[20]	43[21]		
Units: Gram per liter				
arithmetic mean (standard deviation)				
IgA	0.0768 (± 0.91109)	0.054 (± 0.23643)		
IgG	-0.714 (± 3.0614)	-1.246 (± 5.3194)		
IgM	-0.049 (± 0.29267)	-0.0463 (± 0.16294)		

Notes:

[20] - Safety Population. Only participants who were available at the indicated time points were analyzed

[21] - Safety Population. Only participants who were available at the indicated time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cluster of differentiation (CD) CD5+CD19+ cell counts up to 36 months

End point title	Change from Baseline in cluster of differentiation (CD) CD5+CD19+ cell counts up to 36 months

End point description:

CD5+ CD19+ cells were counted by flow cytometry. Flow cytometry is a technique for counting and examining microscopic particles with an electronic detection apparatus. Baseline CD5+ CD19+ cell count value is the last pre-dose assessment values performed on cycle 1 Day 1. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline, 3-Month Follow-up to 36-Month Follow-up (in 3 months interval)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[22]	53[23]		
Units: Cell per microliter				
arithmetic mean (standard deviation)				
3 month F/U - Baseline (n=32, 31)	-72622.5 (± 104175.69)	-40644.2 (± 36183.14)		
6 month F/U - Baseline (n=30,28)	-61258.2 (± 42645.75)	-45630.4 (± 40130.68)		
9 month F/U - Baseline (n=37,23)	-76688.7 (± 99375.55)	-49527.3 (± 40728.82)		
12 month F/U - Baseline (n=32,23)	-77884.8 (± 106795.41)	-43994.3 (± 39165.64)		
15 month F/U - Baseline (n=29,21)	-80997.6 (± 108950.32)	-39985.6 (± 36456.16)		
18 month F/U - Baseline (n=23,11)	-85837.7 (± 120525.82)	-31229.5 (± 28486.65)		
21 month F/U - Baseline (n=17,8)	-82180.6 (± 138188.36)	-52665.1 (± 42250.59)		
24 month F/U - Baseline (n=15,7)	-92850.6 (± 144547.27)	-37969.3 (± 26444.26)		
27 month F/U - Baseline (n=19, 6)	-82553.4 (± 129930.36)	-24824.8 (± 23700.4)		
30 month F/U - Baseline (n=15, 6)	-96903.7 (± 142080.38)	-30938 (± 28108.7)		
33 month F/U - Baseline (n=10, 3)	-65321.8 (± 40537.06)	-38216.3 (± 24864.31)		
36 month F/U - Baseline (n=8, 4)	-52087.1 (± 35735.07)	-30961 (± 25003.73)		

Notes:

[22] - ATS Population. Only participants with data available at the specified time points were analyzed

[23] - ATS Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cluster of differentiation (CD) CD5-CD19+ cell counts up to 36 months

End point title	Change from Baseline in cluster of differentiation (CD) CD5-CD19+ cell counts up to 36 months

End point description:

CD5-CD19+ cells were counted by flow cytometry. Flow cytometry is a technique for counting and examining microscopic particles with an electronic detection apparatus. Baseline CD5- CD19+ cell count value is the last pre-dose assessment values performed on cycle 1 Day 1. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline, 3-Month Follow-up to 36-Month Follow-up (in 3 months interval)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[24]	53[25]		
Units: Cell per microliter				
arithmetic mean (standard deviation)				
3 month F/U - Baseline (n= 32, 31)	-5800.8 (± 12693.09)	-2052.4 (± 5243.64)		
6 month F/U - Baseline (n= 30, 28)	-3921.1 (± 6959.2)	-3822.8 (± 8449.8)		
9 month F/U - Baseline (n= 37, 23)	-5969.7 (± 12277.21)	-2288.4 (± 5724.47)		
12 month F/U - Baseline (n= 32, 23)	-6756.8 (± 13009.04)	-4656.3 (± 9087.98)		
15 month F/U - Baseline (n= 29, 21)	-5323.6 (± 8727.91)	-4256.2 (± 9145.23)		
18 month F/U - Baseline (n= 23, 11)	-4677.9 (± 7677.12)	-5043.6 (± 10927.98)		
21 month F/U - Baseline (n= 17, 8)	-5224.2 (± 8477.84)	-275.1 (± 449.28)		
24 month F/U - Baseline (n= 15, 7)	-4522.7 (± 7562.59)	-224 (± 447.47)		
27 month F/U - Baseline (n= 19, 6)	-7259 (± 10162.96)	-3870.5 (± 8960.8)		
30 month F/U - Baseline (n= 15, 6)	-7673.6 (± 10238.82)	-3964.3 (± 8918.4)		
33 month F/U - Baseline (n= 10, 3)	-9511.2 (± 11834.25)	-206 (± 215.84)		
36 month F/U - Baseline (n= 8, 4)	-8430.1 (± 13019.82)	-5693 (± 10969)		

Notes:

[24] - ATS Population. Only participants with data available at the specified time points were analyzed

[25] - ATS Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who were negative or positive for minimal residual disease (MRD) and achieved a bone marrow biopsy confirmed complete response (CR) up to 36-Month Follow-up

End point title	Number of participants who were negative or positive for minimal residual disease (MRD) and achieved a bone marrow biopsy confirmed complete response (CR) up to 36-Month Follow-up

End point description:

MRD refers to small number of leukemic cells that remain in the participant during treatment or after treatment at the time the participant achieved a confirmed CR. MRD analysis was performed for the partcipants who were suspected of achieving a primary endpoint CR. Analysis of CD5+ CD19+ was performed on the bone marrow aspirate sample obtained no sooner than 2 months following the last dose of study treatment. MRD results were reported as negative or positive. The absence of MRD (negative MRD) is defined as less than one CLL cell per 10000 leukocytes.

End point type	Secondary

End point timeframe:

3 month follow up to the 36 Month Follow-up (in 3 month interval)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[26]	4[27]		
Units: Participants				
3 month F/U, MRD Positive (n=16 , 4)	7	4		
3 month F/U, MRD Negative (n=16 , 4)	9	0		
6 month F/U, MRD Positive (n=8 , 2)	1	1		
6 month F/U, MRD Negative (n=8 , 2)	7	1		
9 month F/U, MRD Positive (n=11 , 2)	3	1		
9 month F/U, MRD Negative (n=11 , 2)	8	1		
12 month F/U, MRD Positive (n=9 , 2)	1	1		
12 month F/U, MRD Negative (n=9 , 2)	8	1		
15 month F/U, MRD Positive (n=9 , 2)	3	1		
15 month F/U, MRD Negative (n=9 , 2)	6	1		
18 month F/U, MRD Positive (n=6 , 1)	1	0		
18 month F/U, MRD Negative (n=6 , 1)	5	1		
21 month F/U, MRD Positive (n=7, 1)	2	0		
21 month F/U, MRD Negative (n=7 , 1)	5	1		
24 month F/U, MRD Positive (n=6 , 1)	0	0		
24 month F/U, MRD Negative (n=6 , 1)	6	1		
27 month F/U, MRD Positive (n=3 , 1)	0	0		
27 month F/U, MRD Negative (n=3 , 1)	3	1		
30 month F/U, MRD Positive (n=4 , 1)	1	0		
30 month F/U, MRD Negative (n=4 , 1)	3	1		
33 month F/U, MRD Positive (n=4 , 1)	1	0		
33 month F/U, MRD Negative (n=4 , 1)	3	1		
36 month F/U, MRD Positive (n=2 , 1)	0	0		
36 month F/U, MRD Negative (n=2 , 1)	2	1		

Notes:

[26] - ATS Population. Number of subjects who had CR with bone marrow confirmation are included

[27] - ATS Population. Number of subjects who had CR with bone marrow confirmation are included

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who received no transfusion or at least one transfusion during the study

End point title	Number of participants who received no transfusion or at least one transfusion during the study

End point description:

Participants who received no transfusion and at least one transfusion during the study are presented. Participants who took any blood products are counted in this table.

End point type	Secondary

End point timeframe:

From start of treatment until earliest date of disease progression or death (up to 3 years after the last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[28]	53[29]		
Units: Participants				
No transfusions	38	33		
At least one transfusion	6	20		

Notes:

[28] - Safety Population: All subjects who receive at least one dose of study medication.

[29] - Safety Population: All subjects who receive at least one dose of study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with autoimmune hemolytic anaemia (AIHA) disease

End point title	Number of participants with autoimmune hemolytic anaemia (AIHA) disease

End point description:

AIHA is a disease where the body's immune system fails to recognize red blood cells as "self" and begins destroying these red blood cells. The number of participants diagnosed with AIHA are presented.

End point type	Secondary

End point timeframe:

From first dose of study medication to 60 days after the last dose of study medication (if the event is considered as an AE), or up to 3 years after the last dose of study treatment or until the time of the next anti-CLL therapy, if considered a SAE

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[30]	53[31]		
Units: Participants	0	1		

Notes:

[30] - Safety Population: All subjects who receive at least one dose of study medication.

[31] - Safety Population: All subjects who receive at least one dose of study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Grade 3 or Grade 4 myelosuppression (anemia, neutropenia, and thrombocytopenia), as assessed by the investigator

End point title	Number of participants with the indicated Grade 3 or Grade 4 myelosuppression (anemia, neutropenia, and thrombocytopenia), as assessed by the investigator

End point description:

Participants with a Grade 3 or Grade 4 myelosuppression (anemia, neutropenia, and thrombocytopenia) are presented. Myelosuppression is defined as the decrease in the ability of the bone marrow to produce blood cells. AEs were graded according to NCI common terminology criteria for adverse events (CTCAE) grade, version 4.0 (1, mild; 2, moderate; 3, severe; 4, life-threatening/disabling; 5, death).

End point type	Secondary

End point timeframe:

From the first dose of study medication to 60 days after the last dose of study medication

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[32]	53[33]		
Units: Participants				
Neutropenia/Febrile neutropenia, Grade 3	8	27		
Neutropenia/Febrile Neutropenia, Grade 4	9	16		
Thrombocytopenia, Grade 3	1	2		
Thrombocytopenia, Grade 4	0	2		
Anemia, Grade 3	1	0		
Anemia, Grade 4	0	0		

Notes:

[32] - From the first dose of study medication to 60 days after the last dose of study medication

[33] - From the first dose of study medication to 60 days after the last dose of study medication

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Grade 3 or Grade 4 adverse event of infection

End point title	Number of participants with the indicated Grade 3 or Grade 4 adverse event of infection

End point description:

Participants with the indicated Grade 3 or Grade 4 adverse event of infection are presented. AEs were graded according to the NCI CTCAE grade, version 4.0 (1, mild; 2, moderate; 3, severe; 4, life-threatening/disabling; 5, death).

End point type	Secondary

End point timeframe:

From first dose of study medication to 60 days after the last dose of study medication (if the event is considered as an AE), or up to 3 years after the last dose of study treatment or until the time of the next anti-CLL therapy, if considered a SAE

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[34]	53[35]		
Units: Participants	5	10		

Notes:

[34] - Safety Population: All subjects who receive at least one dose of study medication.

[35] - Safety Population: All subjects who receive at least one dose of study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated constitutional or B-symptoms

End point title	Number of participants with the indicated constitutional or B-symptoms

End point description:

Participants with the indicated constitutional or B-symptoms (night sweats, weight loss, fever or extreme fatigue) were presented for different time points.

End point type	Secondary

End point timeframe:

Screening (SCR), Cycle 3 Day 1 (C3D1), Cycle 6 Day 1 (C6D1), 12, 24 and 36 Month Follow-up (F/U)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[36]	53[37]		
Units: Participants				
SCR, night sweats, n =44, 52	19	22		
SCR, weight loss, n=44, 52	4	5		
SCR, fever, n=44, 52	1	2		
SCR, extreme fatigue, n=44, 52	14	15		
C3D1, night sweats, n =42, 49	5	2		
C3D1, weight loss, n=42, 49	0	2		
C3D1, fever, n=42, 49	0	0		
C3D1, extreme fatigue, n=42, 49	2	4		
C6D1, night sweats, n =39, 47	0	1		
C6D1, weight loss, n =39, 47	0	0		
C6D1, fever, n =39, 47	0	0		
C6D1, extreme fatigue, n =39, 47	0	1		
12 Month F/U, night sweats, n =39, 29	0	0		
12 Month F/U, weight loss, n =39, 29	1	0		
12 Month F/U, fever, n =39, 29	0	0		
12 Month F/U, extreme fatigue, n =39, 29	0	0		
24 Month F/U, night sweats, n =29, 17	0	0		
24 Month F/U, weight loss, n=29, 17	0	0		
24 Month F/U, fever, n=29, 17	0	0		

24 Month F/U, extreme fatigue, n=29, 17	1	0		
36 Month F/U, night sweats, n =21, 9	0	0		
36 Month F/U, weight loss, n=21, 9	0	0		
36 Month F/U, fever, n=21, 9	0	0		
36 Month F/U, extreme fatigue, n=21, 9	0	0		

Notes:

[36] - Safety population: Only participants with data available at the specified time points were analyzed

[37] - Safety population: Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated eastern cooperative oncology group (ECOG) performance status (PS)

End point title	Number of participants with the indicated eastern cooperative oncology group (ECOG) performance status (PS)

End point description:

The ECOG performance status scales and criteria are used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living abilities of the participant, and determine appropriate treatment and prognosis. Grade 0, fully active, able to carry on all pre-disease performance without restriction. Grade 1, restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work. Grade 2, ambulatory and capable of all selfcare, but unable to carry out any work activities; up and about more than 50% of waking hours. Grade 3, capable of only limited selfcare; confined to bed or chair more than 50% of waking hours. Grade 4, completely disabled; cannot carry on any selfcare; totally confined to bed or chair. Grade 5, dead.

End point type	Secondary

End point timeframe:

Baseline (BL), Cycle 3 Day 1 (C3D1), Cycle 6 Day 1 (C6D1), 12, 24 and 36 month follow up (F/U)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[38]	53[39]		
Units: Participants				
BL, Score of 0, n=44, 53	16	23		
BL, Score of 1, n=44, 53	28	29		
BL, Score of 2, n=44, 53	0	1		
BL, Score of 3, n=44, 53	0	0		
BL, Score of 4-5, n=44, 53	0	0		
C3D1, Score of 0, n=42, 48	17	27		
C3D1, Score of 1, n=42, 48	25	21		
C3D1, Score of 2, n=42, 48	0	0		
C3D1, Score of 3, n=42, 48	0	0		
C3D1, Score of 4-5, n=42, 48	0	0		
C6D1, Score of 0, n=38, 47	19	27		
C6D1, Score of 1, n=38, 47	19	19		
C6D1, Score of 2, n=38, 47	0	1		
C6D1, Score of 3, n=38, 47	0	0		
C6D1, Score of 4-5, n=38, 47	0	0		

12 Month F/U, Score of 0, n=39, 28	24	19		
12 Month F/U, Score of 1, n=39, 28	14	8		
12 Month F/U, Score of 2, n=39, 28	1	1		
12 Month F/U, Score of 3, n=39, 28	0	0		
12 Month F/U, Score of 4-5, n=39, 28	0	0		
24 Month F/U, Score of 0, n=28, 16	16	13		
24 Month F/U, Score of 1, n=28, 16	11	3		
24 Month F/U, Score of 2, n=28, 16	1	0		
24 Month F/U, Score of 3, n=28, 16	0	0		
24 Month F/U, Score of 4-5, n=28, 16	0	0		
36 Month F/U, Score of 0, n=21, 9	15	8		
36 Month F/U, Score of 1, n=21, 9	5	1		
36 Month F/U, Score of 2, n=21, 9	1	0		
36 Month F/U, Score of 3, n=21, 9	0	0		
36 Month F/U, Score of 4-5, n=21, 9	0	0		

Notes:

[38] - Safety population: Only participants with data available at the specified time points were analyzed

[39] - Safety population: Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with confirmed positive response for human anti-human Antibodies (HAHA) at the indicated time points

End point title	Number of participants with confirmed positive response for human anti-human Antibodies (HAHA) at the indicated time points

End point description:

The presence of HAHA in human serum was determined using a validated electrochemiluminescent assay in a multi-tier assay format. All samples were first assessed in a screening (SCR) assay, and the potential positive (Pos) samples were further tested in the confirmation (CNF) assays. Confirmed positives were reported as HAHA positive and titer was determined for each positive sample. The drug tolerance of the HAHA assay is 200 microgram/milliliter (µg/mL); thus, samples that tested negative in the assay and had ofatumumab concentrations no more than 200 µg/mL were considered as conclusive negative (C Neg) results.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (C1D1), Cycle 6 Day 1 (C6D1), 6-Month Follow-up (F/U), and any post-dose time point

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[40]	53[41]		
Units: Participants				
C1D1, n=41, 53	0	0		
C6D1, n=34, 43	0	0		
6-Month F/U, n=35, 37	0	0		
Any post dose time, n=42, 47	0	0		

Notes:

[40] - Safety population: Only participants with data available at the specified time points were analyzed

[41] - Safety population: Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum decrease in sum of the product of the diameter (SPD) from Baseline in participants with lymphadenopathy at Baseline

End point title	Maximum decrease in sum of the product of the diameter (SPD) from Baseline in participants with lymphadenopathy at Baseline

End point description:

Lymph nodes were evaluated by physical examination which involved recording the diameter in two planes (sum of the product of the diameter [SPD]) of the largest palpable node in each of the following sites: cervical, axillary, supraclavicular, inguinal and femoral. Lymphadenopathy is defined as lymph nodes with the largest diameter greater than 1.5 centimeters. The maximum reduction in SPD from Baseline at C2D1, C3D1, C4D1, C5D1, C6D1, 3-Month F/U, 6-Month F/U and 9-Month F/U are provided.

End point type	Secondary

End point timeframe:

Baseline, Cycle 2 Day 1 (C2D1), Cycle 3 Day 1 (C3D1), Cycle 4 Day 1 (C4D1), Cycle 5 Day 1 (C5D1), Cycle 6 Day 1 (C6D1), 3-Month Follow-Up (F/U), 6-Month F/U and 9-Month F/U

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[42]	53[43]		
Units: cm^2 (centimeters squared)				
arithmetic mean (standard deviation)				
C2D1, n=34, 35	-83.5 (± 23.69)	-77.3 (± 31.62)		
C3D1, n=32, 35	-92.1 (± 20.17)	-90.9 (± 17.18)		
C4D1, n=32, 35	-99.1 (± 2.67)	-94.6 (± 11.56)		
C5D1, n=29, 35	-99.6 (± 1.22)	-96.2 (± 8.95)		
C6D1, n=30, 33	-99.6 (± 2.28)	-97 (± 7.78)		
3-Month F/U, n=33, 32	-99.2 (± 3.64)	-95.9 (± 19.17)		
6-Month F/U, n=3, 1	-100 (± 0)	-100 (± 99999.999)		
9-Month F/U, n=1, 0	-68.4 (± 99999.999)	99999.99 (± 99999.99)		

Notes:

[42] - Safety population: Only participants with data available at the specified time points were analyzed

[43] - Safety population: Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated reduction in organomegaly (spleen and liver)

End point title	Number of participants with the indicated reduction in organomegaly (spleen and liver)

End point description:

Organomegaly is the abnormal enlargement of organs. Physical examination of the liver (L) and spleen (S) were done at Screening (SCR), C3D1, C6D1, 12-Month F/U, 24-Month F/U and 36-Month F/U. The result of the physical examination of the liver (L) and spleen (S) was presented as normal (NOR), enlarged (EL) and not assessed (NOA).

End point type	Secondary

End point timeframe:

Screening (Scr), Cycle 3 Day 1 (C3D1), Cycle 6 Day 1 (C6D1), 12, 24 and 36 -Month Follow-Up (F/U)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[44]	53[45]		
Units: Participants				
SCR, S, NOR, n=44, 50	23	31		
SCR, S, EL, n=44, 50	21	19		
SCR, S, NOA, n=44, 50	0	0		
SCR, L, NOR, n=44, 51	38	41		
SCR, L, EL, n=44, 51	6	9		
SCR, L, NOA, n=44, 51	0	1		
C3D1, S, NOR, n=42, 48	37	41		
C3D1, S, EL, n=42, 48	5	6		
C3D1, S, NOA, n=42, 48	0	1		
C3D1, L, NOR, n=42, 48	38	42		
C3D1, L, EL, n=42, 48	4	5		
C3D1, L, NOA, n=42, 48	0	1		
C6D1, S, NOR, n=39, 46	39	43		
C6D1, S, EL, n=39, 46	0	2		
C6D1, S, NOA, n=39, 46	0	1		
C6D1, L, NOR, n=39, 46	37	44		
C6D1, L, EL, n=39, 46	2	0		
C6D1, L, NOA, n=39, 46	0	2		
12 Month F/U, S, NOR, n=39, 29	39	28		
12 Month F/U, S, EL, n=39, 29	0	1		
12 Month F/U, S, NOA, n=39, 29	0	0		
12 Month F/U, L, NOR, n=39, 29	38	28		
12 Month F/U, L, EL, n=39, 29	1	1		
12 Month F/U, L, NOA, n=39, 29	0	0		
24 Month F/U, S, NOR, n=29, 17	29	16		
24 Month F/U, S, EL, n=29, 17	0	1		
24 Month F/U, S, NOA, n=29, 17	0	0		
24 Month F/U, L, NOR, n=29, 17	29	16		
24 Month F/U, L, EL, n=29, 17	0	1		

24 Month F/U, L, NOA, n=29, 17	0	0		
36 Month F/U, S, NOR, n=21, 9	21	9		
36 Month F/U, S, EL, n=21, 9	0	0		
36 Month F/U, S, NOA, n=21, 9	0	0		
36 Month F/U, L, NOR, n=21, 9	21	9		
36 Month F/U, L, EL, n=21, 9	0	0		
36 Month F/U, L, NOA, n=21, 9	0	0		

Notes:

[44] - Safety Population. Only participants with data available at the specified time points were analyzed

[45] - Safety Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated cytogenetics testing at Baseline who also had a clinical response after last dose of study treatment

End point title	Number of participants with the indicated cytogenetics testing at Baseline who also had a clinical response after last dose of study treatment

End point description:

Cytogenetics refers to the study of numerical and structural chromosomal abnormalities. Cytogenetics (analyzed by fluorescent in situ hybridization [FISH]) of 17p deletion, 11q deletion, 17p or 11q deletions, 6q- or +12q or 13q- deletions, and no aberration at Baseline were summarized by clinical responses after the last dose of study treatment. Clinical responses included complete remission (CR), nodular partial remission (nPR), complete response with incomplete bone marrow Recovery (CRi), partial remission (PR), disease progression (PD), and stable disease (SD). The participants with a PR, CRi, PR or nPR are called responders and the participants with SD and PD are called non-responders.

End point type	Secondary

End point timeframe:

From the start of study treatment until earliest date of disease progression or death (up to up to 3 months following last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[46]	53[47]		
Units: Participants				
17p-, CR, n=2, 6	0	0		
17p-, CRi, n=2, 6	0	0		
17p-, nPR, n=2, 6	0	0		
17p-, PR, n=2, 6	0	1		
17p-, SD, n=2, 6	1	3		
17p-, PD, n=2, 6	0	2		
11q-, CR, n=8, 15	3	1		
11q-, CRi, No, n=8, 15	0	0		
11q-, nPR, n=8, 15	1	3		
11q-, PR, n=8, 15	4	7		
11q-, SD, n=8, 15	0	1		
11q-, PD, n=8, 15	0	3		
17p- or 11q-, CR, n=10, 20	3	1		

17p- or 11q-, CRi, n=10, 20	0	0		
17p- or 11q-, nPR, n=10, 20	1	3		
17p- or 11q-, PR, n=10, 20	4	8		
17p- or 11q-, SD, n=10, 20	1	3		
17p- or 11q-, PD, n=10, 20	0	5		
6q- or +12q or 13q-, CR, n=20, 24	11	3		
6q- or +12q or 13q-, CRi, n=20, 24	1	2		
6q- or +12q or 13q-, nPR, n=20, 24	1	4		
6q- or +12q or 13q-, PR, n=20, 24	7	10		
6q- or +12q or 13q-, SD, n=20, 24	0	2		
6q- or +12q or 13q-, PD, n=20, 24	0	2		
No aberration, CR, n= 14, 8	5	2		
No aberration, CRi, n= 14, 8	2	0		
No aberration, nPR, n= 14, 8	3	1		
No aberration, PR, n= 14, 8	4	4		
No aberration, SD, n= 14, 8	0	0		
No aberration, PD, n= 14, 8	0	1		

Notes:

[46] - Safety Population. Only participants with data available at the specified time points were analyzed

[47] - Safety Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Beta 2 microglobulin (B2M) at Baseline who also had a clinical response after the last dose of study treatment

End point title	Number of participants with the indicated Beta 2 microglobulin (B2M) at Baseline who also had a clinical response after the last dose of study treatment

End point description:

Participants with B2M concentration of <=4000 µg/L and >4000 µg/L at Baseline and who had clinical response after the last dose of study treatment were provided. Clinical responses included complete remission (CR), complete response with incomplete bone marrow Recovery (CRi), nodular partial remission (nPR), and partial remission (PR), disease progression (PD), and stable disease (SD). The participants with a PR, CRi, PR or nPR are called responders and the participants with SD and PD are called non-responders.

End point type	Secondary

End point timeframe:

From the start of study treatment until earliest date of disease progression or death (up to up to 3 months following last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[48]	53[49]		
Units: Participants				
<= 4000 µg/L, CR, n=23, 24	9	3		
<= 4000 µg/L, CRi, n=23, 24	3	2		
<= 4000 µg/L, nPR, n=23, 24	4	6		
<= 4000 µg/L, PR, n=23, 24	7	9		

<= 4000 µg/L, SD, n=23, 24	0	2		
<= 4000 µg/L, PD, n=23, 24	0	2		
> 4000 µg/L, CR, n=17, 29	9	3		
> 4000 µg/L, CRi, n=17, 29	0	0		
> 4000 µg/L, nPR, n=17, 29	1	2		
> 4000 µg/L, PR, n=17, 29	6	14		
> 4000 µg/L, SD, n=17, 29	0	3		
> 4000 µg/L, PD, n=17, 29	0	6		

Notes:

[48] - ATS Population. Only participants with data available at the specified time points were analyzed

[49] - ATS Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated immunoglobulin heavy chain variable region (IgVH) testing at Baseline who also had a clinical response after last dose of study treatment

End point title	Number of participants with the indicated immunoglobulin heavy chain variable region (IgVH) testing at Baseline who also had a clinical response after last dose of study treatment

End point description:

Participants with IgVH mutation results as mutated and unmutated status and clinical response after last dose of study treatment were provided. Clinical responses included complete remission (CR), complete response with incomplete bone marrow recovery (CRi), nodular partial remission (nPR), partial remission (PR), disease progression (PD), and stable disease (SD). The participants with a PR, CRi, PR or nPR are called responders and the participants with SD and PD are called non-responders.

End point type	Secondary

End point timeframe:

From the start of study treatment until earliest date of disease progression or death (up to up to 3 months following last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[50]	53[51]		
Units: Participants				
IgVH Mutated (<=98 %), CR, n=12, 13	6	4		
IgVH Mutated (<=98 %), CRi, n=12, 13	2	0		
IgVH Mutated (<=98 %), nPR, n=12, 13	0	4		
IgVH Mutated (<=98 %), PR, n=12, 13	4	2		
IgVH Mutated (<=98 %), SD, n=12, 13	0	0		
IgVH Mutated (<=98 %), PD, n=12, 13	0	3		
IgVH unmutated (>98%), CR, n=23, 34	11	1		
IgVH unmutated (>98%), CRi, n=23, 34	1	2		
IgVH unmutated (>98%), nPR, n=23, 34	5	4		
IgVH unmutated (>98%), PR, n=23, 34	5	18		
IgVH unmutated (>98%), SD, n=23, 34	0	5		
IgVH unmutated (>98%), PD, n=23, 34	0	3		

Notes:

[50] - ATS Population. Only participants with data available at the specified time points were analyzed

[51] - ATS Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with zeta-chain-associated protein kinase (ZAP) 70 testing at Baseline who also had a clinical response after last dose of study treatment

End point title	Number of participants with zeta-chain-associated protein kinase (ZAP) 70 testing at Baseline who also had a clinical response after last dose of study treatment

End point description:

ZAP-70 is a protein normally expressed near the surface membrane of T cells and natural killer cells. ZAP-70 in B cells is used as a prognostic marker in identifying different forms of CLL. Participants with ZAP-70 testing results intermediate (Int), positive (Pos) and negative (Neg) at Baseline and who had a clinical response after last dose of study treatment are provided. Clinical responses included complete remission (CR), complete response with incomplete bone marrow recovery (CRi), nodular partial remission (nPR), partial remission (PR), disease progression (PD), and stable disease (SD). The participants with a PR, CRi, PR or nPR are called responders and the participants with SD and PD are called non-responders.

End point type	Secondary

End point timeframe:

From the start of study treatment until earliest date of disease progression or death (up to 3 months following last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[52]	44[53]		
Units: Participants				
ZAP-70, Int, CR, n=6, 6	1	1		
ZAP-70, Int, CRi, n=6, 6	0	0		
ZAP-70, Int, nPR, n=6, 6	0	0		
ZAP-70, Int, PR, n=6, 6	3	3		
ZAP-70, Int, PD, n=6, 6	0	1		
ZAP-70, Int, SD, n=6, 6	1	0		
ZAP-70, Neg, CR, n=2, 2	1	0		
ZAP-70, Neg, CRi, n=2, 2	0	0		
ZAP-70, Neg, nPR, n=2, 2	0	0		
ZAP-70, Neg, PR, n=2, 2	1	2		
ZAP-70, Neg, PD, n=2, 2	0	0		
ZAP-70, Neg, SD, n=2, 2	0	0		
ZAP-70, Pos, CR, n=36, 44	17	5		
ZAP-70, Pos, CRi, n=36, 44	3	2		
ZAP-70, Pos, nPR, n=36, 44	5	8		
ZAP-70, Pos, PR, n=36, 44	11	17		

ZAP-70, Pos, PD, n=36, 44	0	7		
ZAP-70, Pos, SD, n=36, 44	0	5		

Notes:

[52] - ATS Population. Only participants with data available at the specified time points were analyzed

[53] - ATS Population. Only participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with an adverse event of any infusion reactions (IR) or serious infusion reactions (SIR)

End point title	Number of participants with an adverse event of any infusion reactions (IR) or serious infusion reactions (SIR)

End point description:

An Infusion reaction is defined as events occurring after the beginning of an infusion of ofatumumab or within 24 hours following the end of an infusion of bendamustine.

End point type	Secondary

End point timeframe:

From the first dose of study medication to 60 days after the last dose of study medication (up to 24 hours after last dose of study treatment)

End point values	Ofatumumab + Bendamustine 90 mg/m^2	Ofatumumab + Bendamustine 70 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[54]	53[55]		
Units: Participants				
Any ofatumumab only IR	30	34		
Any ofatumumab only SIR	3	4		
Any ofatumumab plus bendamustine IR	30	35		
Any ofatumumab plus bendamustine SIR	4	4		

Notes:

[54] - Safety Population: All subjects who receive at least one dose of study medication.

[55] - Safety Population: All subjects who receive at least one dose of study medication.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Ofatumumab + Bendamustine 70mg/m^2

Reporting group description:

Participants with relapsed CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 70 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Reporting group title	Ofatumumab + Bendamustine 90mg/m^2

Reporting group description:

Participants with previously untreated CLL received IV infusions of ofatumumab in combination with bendamustine IV infusions for 6 cycles; each cycle comprised of 28 days. Participants received ofatumumab administered at 300 mg on Day 1, 1000 mg on Day 8 of cycle 1 and 1000 mg on Day 1 of cycles 2, 3, 4, 5 and 6. Bendamustine was administered at 90 mg/m^2 on Days 1 and 2 of each cycle (6 cycles).

Serious adverse events	Ofatumumab + Bendamustine 70mg/m^2	Ofatumumab + Bendamustine 90mg/m^2	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 53 (47.17%)	20 / 44 (45.45%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bowen's disease			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 53 (1.89%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 53 (0.00%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 53 (3.77%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 53 (3.77%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 44 (6.82%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	4 / 53 (7.55%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	1 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Neutropenia			
subjects affected / exposed	3 / 53 (5.66%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	5 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Chills			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 53 (5.66%)	3 / 44 (6.82%)	
occurrences causally related to treatment / all	5 / 5	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Type IV hypersensitivity reaction			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 53 (3.77%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 53 (3.77%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelothrix infection			

subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 53 (5.66%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			

subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection bacterial			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 53 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Ofatumumab + Bendamustine 70mg/m^2	Ofatumumab + Bendamustine 90mg/m^2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 53 (92.45%)	40 / 44 (90.91%)	
Vascular disorders			
Flushing			
subjects affected / exposed	5 / 53 (9.43%)	1 / 44 (2.27%)	
occurrences (all)	6	1	
Phlebitis			
subjects affected / exposed	0 / 53 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 53 (5.66%)	5 / 44 (11.36%)	
occurrences (all)	4	6	
Chills			
subjects affected / exposed	3 / 53 (5.66%)	5 / 44 (11.36%)	
occurrences (all)	4	5	
Fatigue			
subjects affected / exposed	8 / 53 (15.09%)	7 / 44 (15.91%)	
occurrences (all)	10	8	
Malaise			
subjects affected / exposed	4 / 53 (7.55%)	0 / 44 (0.00%)	
occurrences (all)	4	0	
Oedema peripheral			
subjects affected / exposed	4 / 53 (7.55%)	3 / 44 (6.82%)	
occurrences (all)	5	8	
Pyrexia			
subjects affected / exposed	8 / 53 (15.09%)	10 / 44 (22.73%)	
occurrences (all)	13	12	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 53 (7.55%)	3 / 44 (6.82%)	
occurrences (all)	4	3	
Dyspnoea			

subjects affected / exposed	3 / 53 (5.66%)	5 / 44 (11.36%)	
occurrences (all)	3	6	
Oropharyngeal pain			
subjects affected / exposed	3 / 53 (5.66%)	1 / 44 (2.27%)	
occurrences (all)	3	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 53 (3.77%)	6 / 44 (13.64%)	
occurrences (all)	3	7	
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 53 (5.66%)	3 / 44 (6.82%)	
occurrences (all)	3	3	
Weight decreased			
subjects affected / exposed	3 / 53 (5.66%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	8 / 53 (15.09%)	3 / 44 (6.82%)	
occurrences (all)	15	24	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 53 (5.66%)	5 / 44 (11.36%)	
occurrences (all)	4	6	
Headache			
subjects affected / exposed	6 / 53 (11.32%)	6 / 44 (13.64%)	
occurrences (all)	8	10	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 53 (9.43%)	5 / 44 (11.36%)	
occurrences (all)	5	5	
Neutropenia			
subjects affected / exposed	32 / 53 (60.38%)	20 / 44 (45.45%)	
occurrences (all)	62	50	
Thrombocytopenia			

subjects affected / exposed	12 / 53 (22.64%)	7 / 44 (15.91%)	
occurrences (all)	16	11	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 53 (5.66%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Abdominal pain upper			
subjects affected / exposed	4 / 53 (7.55%)	5 / 44 (11.36%)	
occurrences (all)	5	9	
Constipation			
subjects affected / exposed	5 / 53 (9.43%)	6 / 44 (13.64%)	
occurrences (all)	6	9	
Diarrhoea			
subjects affected / exposed	7 / 53 (13.21%)	5 / 44 (11.36%)	
occurrences (all)	8	7	
Nausea			
subjects affected / exposed	16 / 53 (30.19%)	19 / 44 (43.18%)	
occurrences (all)	21	27	
Vomiting			
subjects affected / exposed	4 / 53 (7.55%)	5 / 44 (11.36%)	
occurrences (all)	5	7	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	5 / 53 (9.43%)	3 / 44 (6.82%)	
occurrences (all)	5	3	
Erythema			
subjects affected / exposed	2 / 53 (3.77%)	3 / 44 (6.82%)	
occurrences (all)	5	3	
Pruritus			
subjects affected / exposed	4 / 53 (7.55%)	7 / 44 (15.91%)	
occurrences (all)	6	7	
Rash			
subjects affected / exposed	7 / 53 (13.21%)	12 / 44 (27.27%)	
occurrences (all)	9	20	
Urticaria			

subjects affected / exposed	3 / 53 (5.66%)	6 / 44 (13.64%)	
occurrences (all)	4	10	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 44 (9.09%)	
occurrences (all)	2	4	
Back pain			
subjects affected / exposed	3 / 53 (5.66%)	5 / 44 (11.36%)	
occurrences (all)	3	5	
Bone pain			
subjects affected / exposed	0 / 53 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	6	
Pain in extremity			
subjects affected / exposed	3 / 53 (5.66%)	1 / 44 (2.27%)	
occurrences (all)	3	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 53 (5.66%)	2 / 44 (4.55%)	
occurrences (all)	4	2	
Herpes simplex			
subjects affected / exposed	3 / 53 (5.66%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	3 / 53 (5.66%)	1 / 44 (2.27%)	
occurrences (all)	4	1	
Upper respiratory tract infection			
subjects affected / exposed	5 / 53 (9.43%)	3 / 44 (6.82%)	
occurrences (all)	5	3	
Urinary tract infection			
subjects affected / exposed	2 / 53 (3.77%)	3 / 44 (6.82%)	
occurrences (all)	3	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 53 (9.43%)	6 / 44 (13.64%)	
occurrences (all)	5	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: