Clinical trial results:
A Phase II, Open-Label Study Evaluating the Safety and Efficacy of GDC-0199 (ABT-199) Plus Bendamustine Plus Rituximab (BR) in Comparison with BR Alone or GDC-0199 Plus Rituximab (R) in Patients with Relapsed and Refractory Follicular Non-Hodgkin's Lymphoma

Summary

EudraCT number	2014-000576-26
Trial protocol	GB IT DE BE FR
Global end of trial date	16 March 2018

Results information

Result version number	v2
This version publication date	20 April 2018
First version publication date	14 October 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BO29337

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02187861
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com

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	Interim
Date of interim/final analysis	06 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 September 2016
Global end of trial reached?	Yes
Global end of trial date	16 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of venetoclax plus BR compared with BR alone and venetoclax plus rituximab in participants with relapsed and refractory follicular lymphoma, as measured by the positron emission tomography (PET) defined complete metabolic response (CMR) at the time of primary response assessment as defined by an Independent Review Committee (IRC)

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) according to the applicable local regulations and policies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 33
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	United States: 34
Worldwide total number of subjects	164
EEA total number of subjects	75

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	86
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The clinical cut-off date for data included in this posting was 06 April 2017.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)

Arm description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	GDC-0199
Other name	ABT-199
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	Levact
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bendamustine was administered as per the schedule specified under arm description.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera, Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

Arm title	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)

Arm description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	GDC-0199
Other name	ABT-199
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera, Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

Arm title	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)

Arm description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	GDC-0199
Other name	ABT-199
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	Levact
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bendamustine was administered as per the schedule specified under arm description.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera, Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

Arm title	Chemotherapy-Containing Cohort: Arm C (BR)

Arm description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Arm type	Active comparator
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	Levact
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Bendamustine was administered as per the schedule specified under arm description.	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera, Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Rituximab was administered as per the schedule specified under arm description.	

Number of subjects in period 1	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax +	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)
Started	9	53	51
Treated	9	52	49
Completed	0	0	0
Not completed	9	53	51
Physician decision	-	1	-
Consent withdrawn by subject	-	-	2
Adverse Event	2	1	3
Death	-	3	1
Progressive Disease	3	35	13
Alive in Study Follow-Up	4	10	26
Unspecified	-	2	6
Lack of efficacy	-	1	-

Number of subjects in period 1	Chemotherapy-Containing Cohort: Arm C (BR)
Started	51
Treated	50
Completed	0
Not completed	51
Physician decision	3
Consent withdrawn by subject	3
Adverse Event	-
Death	2
Progressive Disease	11
Alive in Study Follow-Up	31
Unspecified	1
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

Reporting group title	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Containing Cohort: Arm C (BR)

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax +	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)
Number of subjects	9	53	51
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	57.9	62.0	64.9
standard deviation	± 12.7	± 11.9	± 9.8
Gender Categorical Units: Subjects			
Female	5	26	16
Male	4	27	35

Reporting group values	Chemotherapy-Containing Cohort: Arm C (BR)	Total	
Number of subjects	51	164	
Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	61.0		
standard deviation	± 11.6	-	
Gender Categorical Units: Subjects			
Female	21	68	
Male	30	96	

End points

End points reporting groups

Reporting group title	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

Reporting group title	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Containing Cohort: Arm C (BR)

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Primary: Percentage of Participants with Complete Metabolic Response (CMR) According to Independent Review Committee (IRC) as per Lugano Classification, Using Positron Emission Tomography (PET) Scan at Primary Response Assessment (PRA)

End point title	Percentage of Participants with Complete Metabolic Response (CMR) According to Independent Review Committee (IRC) as per Lugano Classification, Using Positron Emission Tomography (PET) Scan at Primary Response Assessment (PRA)

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake less than or equal to [<=] mediastinum), or 3 (uptake less than [<] mediastinum but <=liver) with or without a residual mass on PET 5-point scale (5-PS), for lymph nodes and extralymphatic sites with no new lesions and no evidence of fluorodeoxyglucose (FDG)-avid disease in bone marrow. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% confidence interval (CI) for percentage of responders was calculated using Clopper-Pearson method. Intent-to-treat (ITT) population included all enrolled participants.

End point type	Primary

End point timeframe:

6-8 weeks after Cycle 6 Day 1 (PRA) (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)	55.6 (21.20 to 86.30)	11.3 (4.27 to 23.03)	74.5 (60.37 to 85.67)	70.6 (56.17 to 82.51)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	3.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.38
upper limit	21.23

Secondary: Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at PRA

End point title	Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at PRA

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

4-10 weeks after Cycle 6 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)	55.6 (21.20 to 86.30)	13.2 (5.48 to 25.34)	68.6 (54.11 to 80.89)	64.7 (50.07 to 77.57)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	3.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.36
upper limit	22.2

Secondary: Percentage of Participants with CMR According to IRC as per Lugano Classification, Using PET Scan at Year 1

End point title	Percentage of Participants with CMR According to IRC as per Lugano Classification, Using PET Scan at Year 1

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (uptake <mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)	55.6 (21.20 to 86.30)	20.8 (10.84 to 34.11)	41.2 (27.58 to 55.83)	39.2 (25.84 to 53.89)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.07
upper limit	20.99

Secondary: Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at Year 1

End point title	Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at Year 1

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)	55.6 (21.20 to 86.30)	17.0 (8.07 to 29.80)	41.2 (27.58 to 55.83)	43.1 (29.35 to 57.75)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.12
upper limit	17.2

Secondary: Percentage of Participants with Complete Response (CR) According to IRC as per Lugano Classification, Using Computed Tomography (CT) Scan

End point title	Percentage of Participants with Complete Response (CR) According to IRC as per Lugano Classification, Using Computed Tomography (CT) Scan

End point description:

CR: defined as reduction of longest transverse diameter of lesion (LDi) of target nodes/nodal masses to <=1.5 centimeters (cm), and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/immunohistochemistry (IHC)-negative bone marrow morphology. Assessment was performed by an IRC according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
6−8 weeks after Cycle 6 Day 1	44.4 (13.70 to 78.80)	5.7 (1.18 to 15.66)	39.2 (25.84 to 53.89)	25.5 (14.33 to 39.63)
Year 1	55.6 (21.20 to 86.30)	13.2 (5.48 to 25.34)	27.5 (15.89 to 41.74)	23.5 (12.79 to 37.49)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
At 6−8 weeks after Cycle 6 Day 1	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	13.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.24
upper limit	31.69

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
At Year 1	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	3.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.98
upper limit	20.82

Secondary: Percentage of Participants with CR According to Investigator as per Lugano Classification, Using CT Scan

End point title	Percentage of Participants with CR According to Investigator as per Lugano Classification, Using CT Scan

End point description:

CR: defined as reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. Assessment was performed by Investigator according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
4-10 weeks after Cycle 6 Day 1	22.2 (2.81 to 60.01)	5.7 (1.18 to 15.66)	15.7 (7.02 to 28.59)	31.4 (19.11 to 45.89)
Year 1	33.3 (7.49 to 70.07)	5.7 (1.18 to 15.66)	13.7 (5.70 to 26.26)	21.6 (11.29 to 35.32)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At 4-10 weeks after Cycle 6 Day 1

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	-15.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.87
upper limit	0.49

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: At Year 1	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in response rates
Point estimate	-7.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.56
upper limit	6.87

Secondary: Percentage of Participants with Objective Response (OR) According to IRC as per Lugano Classification, Using PET Scan

End point title	Percentage of Participants with Objective Response (OR) According to IRC as per Lugano Classification, Using PET Scan

End point description:

OR was defined as CMR or Partial Metabolic Response (PMR). CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. PMR: a score 4 (uptake moderately greater than [>] liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites with no new lesions and reduced residual uptake in bone marrow compared with baseline. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
6−8 weeks after Cycle 6 Day 1	55.6 (21.20 to 86.30)	20.8 (10.84 to 34.11)	76.5 (62.51 to 87.21)	74.5 (60.37 to 85.67)
Year 1	66.7 (29.93 to 92.51)	32.1 (19.92 to 46.32)	45.1 (31.13 to 59.66)	51.0 (36.60 to 65.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET Scan

End point title	Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET Scan

End point description:

OR was defined as CMR or PMR. CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. PMR: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites with no new lesions and reduced residual uptake in bone marrow compared with baseline. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
4-10 weeks after Cycle 6 Day 1	55.6 (21.20 to 86.30)	28.3 (16.79 to 42.35)	76.5 (62.51 to 87.21)	74.5 (60.37 to 85.67)
Year 1	55.6 (21.20 to 86.30)	20.8 (10.84 to 34.11)	41.2 (27.58 to 55.83)	47.1 (32.93 to 61.54)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OR According to IRC as per Lugano Classification, Using CT Scan

End point title	Percentage of Participants with OR According to IRC as per Lugano Classification, Using CT Scan

End point description:

OR was defined as CR or Partial Response (PR). CR: reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. PR: greater than or equal to (>=) 50 percent (%) decrease in sum of the product of the perpendicular diameters (SPD) of up to 6 target measurable nodes and extra-nodal sites; absence/reduction/no increase in size of non-measured lesions; reduction in length of spleen at least >50% beyond normal; and no new lesions. Assessment was performed by an IRC according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
6−8 weeks after Cycle 6 Day 1	66.7 (29.93 to 92.51)	30.2 (18.34 to 44.34)	80.4 (66.88 to 90.18)	84.3 (71.41 to 92.98)
Year 1	66.7 (29.93 to 92.51)	22.6 (12.28 to 36.21)	41.2 (27.58 to 55.83)	60.8 (46.11 to 74.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using CT Scan

End point title	Percentage of Participants with OR According to Investigator as per Lugano Classification, Using CT Scan

End point description:

OR was defined as CR or PR. CR: reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. PR: >=50% decrease in SPD of up to 6 target measurable nodes and extra-nodal sites; absence/reduction/no increase in size of non-measured lesions; reduction in length of spleen at least >50% beyond normal; and no new lesions. Assessment was performed by Investigator according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

End point type	Secondary

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (confidence interval 95%)				
4-10 weeks after Cycle 6 Day 1	55.6 (21.20 to 86.30)	32.1 (19.92 to 46.32)	74.5 (60.37 to 85.67)	78.4 (64.68 to 88.71)
Year 1	55.6 (21.20 to 86.30)	28.3 (16.79 to 42.35)	47.1 (32.93 to 61.54)	49.0 (34.75 to 63.40)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET or CT Scan up to Data Cut-off (06 April 2017)

End point title	Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET or CT Scan up to Data Cut-off (06 April 2017)

End point description:

OR was defined as CMR/CR or PMR/PR. CMR, CR, PMR, and PR have been defined in previous endpoints, and are not repeated here due to space constraint. Assessment was performed by Investigator according to Lugano classification using PET scan or CT scan (if PET is missing). ITT population. 'Number of subjects analysed'=those evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	25	47	47
Units: percentage of participants				
number (not applicable)	33.3	56.0	27.7	31.9

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point title	Duration of Response (DOR) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point description:

DOR was defined as time from CMR/CR or PMR/PR until progressive disease (PD) or death due to any cause. CMR, CR, PMR, and PR have been defined in previous endpoints, and are not repeated here due to space constraint. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan or CT scan (if PET is missing). DOR was calculated using Kaplan-Meier method. ITT population. 'Number of subjects analysed'=those evaluable for this outcome measure. '99999' indicates that upper limit of 95% confidence interval (CI) could not be calculated due to the low number of participants with event.

End point type	Secondary

End point timeframe:

From CMR or PMR until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	25	47	47
Units: months				
median (confidence interval 95%)	16.16 (9.46 to 99999)	14.32 (10.15 to 21.45)	15.18 (10.35 to 99999)	10.61 (9.63 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: Strata were disease burden and DOR of prior cancer therapy.

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.42

Notes:

[1] - Hazard ratio (HR) was calculated using Cox regression.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority[2]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.35

Notes:

[2] - HR was calculated using Cox regression.

Secondary: Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan) or Death

End point title	Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan) or Death

End point description:

PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. ITT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (not applicable)	33.3	75.5	27.5	33.3

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point title	Progression-Free Survival (PFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point description:

PFS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) until the date of disease progression, or death due to any cause. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. PFS was calculated using Kaplan-Meier method. ITT population. '99999' indicates that upper limit of 95% CI could not be calculated due to the low number of participants with event.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: months				
median (confidence interval 95%)	18.83 (12.78 to 99999)	6.57 (6.18 to 12.02)	17.77 (13.37 to 99999)	13.34 (12.25 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: Strata were disease burden and PFS of prior cancer therapy.

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.31

Notes:

[3] - HR was calculated using Cox regression.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.3

Notes:

[4] - HR was calculated using Cox regression.

Secondary: Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan), Death, or Start of a New Anti-lymphoma Therapy

End point title	Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan), Death, or Start of a New Anti-lymphoma Therapy

End point description:

PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. ITT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (not applicable)	33.3	75.5	27.5	33.3

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point title	Event-Free Survival (EFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

End point description:

EFS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) to the date of disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. EFS was calculated using Kaplan-Meier method. ITT population. '99999' indicates that upper limit of 95% CI could not be calculated due to the low number of participants with event.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: months				
median (confidence interval 95%)	18.83 (12.78 to 99999)	6.57 (6.18 to 12.02)	17.77 (13.37 to 99999)	13.34 (12.25 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: Strata were disease burden and EFS of prior cancer therapy.

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.31

Notes:

[5] - HR was calculated using Cox regression.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.3

Notes:

[6] - HR was calculated using Cox regression.

Secondary: Percentage of Participants who Died Due to Any Cause

End point title	Percentage of Participants who Died Due to Any Cause
End point description:	
ITT population	
End point type	Secondary
End point timeframe:	
Baseline until death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])	

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	53	51	51
Units: percentage of participants				
number (not applicable)	0	5.7	2.0	3.9

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) to death due to any cause. For participants who are alive, OS was censored at the last contact. OS was calculated using Kaplan-Meier method. ITT population. '9999' indicates that median and corresponding 95% CI could not be estimated due to higher number of censored participants.

End point type	Secondary

End point timeframe:

Baseline until death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	Chemotherapy-Containing Cohort: Arm C (BR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	3	1	2
Units: months				
median (confidence interval 95%)	(to)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

Notes:

[7] - None of the participants were evaluable as all of them were alive at data cut-off.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: Strata were disease burden and OS of prior cancer therapy.

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)
Number of subjects included in analysis	3
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	5.91

Notes:

[8] - HR was calculated using Cox regression.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Unstratified Analysis

Comparison groups	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR)

Number of subjects included in analysis	3
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	5.63

Notes:

[9] - HR was calculated using Cox regression.

Secondary: Apparent Clearance (CL) of Venetoclax

End point title	Apparent Clearance (CL) of Venetoclax[10]

End point description:

CL is a quantitative measure of the rate at which a drug substance is removed from the body. The data could not be collected as the timepoints for pharmacokinetics collection and the daily dosing of venetoclax did not permit an assessment of CL.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: milliliters per hour (mL/hour)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[11] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

[12] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

[13] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vd) of Venetoclax

End point title	Apparent Volume of Distribution (Vd) of Venetoclax[14]

End point description:

Vd was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. The data could not be collected as the timepoints for pharmacokinetics collection and the daily dosing of venetoclax did not permit an

assessment of Vd.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: milliliters (mL)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[15] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

[16] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

[17] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of Venetoclax

End point title	Time to Maximum Plasma Concentration (Tmax) of

End point description:

Pharmacokinetic-evaluable population included all enrolled participants with available pharmacokinetic data for venetoclax.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	46	
Units: hours				
median (full range (min-max))	8.00 (4.00 to	6.00 (1.95 to	6.21 (1.98 to	

8.08)	8.18)	9.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Venetoclax

End point title	Maximum Plasma Concentration (Cmax) of Venetoclax[19]

End point description:

Pharmacokinetic-evaluable population

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	46	
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	1350 (± 427)	1220 (± 478)	1340 (± 460)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve from Time 0 to Last Observed Concentration (AUClast) of Venetoclax

End point title	Area Under the Plasma Concentration-Time Curve from Time 0 to Last Observed Concentration (AUClast) of Venetoclax[20]

End point description:

Area under the plasma concentration versus time curve from zero to the last measured concentration (AUClast). Pharmacokinetic-evaluable population.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	46	
Units: hours*ng/mL				
arithmetic mean (standard deviation)	5310 (± 1730)	4950 (± 1950)	5500 (± 2270)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve from Time 0 to 8 Hours Post Dose (AUC0-8h) of Venetoclax

End point title	Area Under the Plasma Concentration-Time Curve from Time 0 to 8 Hours Post Dose (AUC0-8h) of Venetoclax[21]

End point description:

Area under the plasma concentration versus time curve from time 0 (pre-dose) to 8 hours post dose (AUC0-8h). Pharmacokinetic-evaluable population. 'Number of subjects analysed'=those evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only applicable for the arms containing venetoclax treatment

End point values	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	30	23	
Units: hours*ng/mL				
arithmetic mean (standard deviation)	5240 (± 1860)	4820 (± 1980)	5330 (± 2270)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 2.5 years (cut-off date 06 April 2017)

Adverse event reporting additional description:

Safety-evaluable population included participants who received at least one dose of any study treatment. 'Related' under this section refers to the adverse events related to venetoclax.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR)

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

Reporting group title	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Reporting group title	Chemotherapy-Containing Cohort: Arm C (BR)

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

Serious adverse events	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax +	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	16 / 52 (30.77%)	24 / 49 (48.98%)
number of deaths (all causes)	0	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Renal stone removal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral stent insertion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplastic anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 52 (0.00%)	6 / 49 (12.24%)
occurrences causally related to treatment / all	2 / 2	0 / 0	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Erosive oesophagitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholelithiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 0	1 / 2	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pyelonephritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Chemotherapy-		

	Containing Cohort: Arm C (BR)		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 50 (20.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Renal stone removal			

subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureteral stent insertion				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Cytokine release syndrome				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 50 (4.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pleuritic pain				

subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute left ventricular failure			

subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Dizziness				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aplastic anaemia				

subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	3 / 50 (6.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Diplopia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erosive oesophagitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute sinusitis			

subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	2 / 50 (4.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster disseminated				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax +	Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab)	Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	49 / 52 (94.23%)	49 / 49 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	3 / 52 (5.77%)	1 / 49 (2.04%)
occurrences (all)	1	3	1
Hypotension			
subjects affected / exposed	2 / 9 (22.22%)	2 / 52 (3.85%)	3 / 49 (6.12%)
occurrences (all)	3	2	5
Orthostatic hypotension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	4 / 52 (7.69%)	5 / 49 (10.20%)
occurrences (all)	1	4	8
Catheter site pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Chills			

subjects affected / exposed	1 / 9 (11.11%)	5 / 52 (9.62%)	4 / 49 (8.16%)
occurrences (all)	1	5	5
Fatigue			
subjects affected / exposed	3 / 9 (33.33%)	13 / 52 (25.00%)	22 / 49 (44.90%)
occurrences (all)	6	14	29
Influenza like illness			
subjects affected / exposed	2 / 9 (22.22%)	1 / 52 (1.92%)	2 / 49 (4.08%)
occurrences (all)	2	1	3
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	3 / 49 (6.12%)
occurrences (all)	0	1	4
Mass			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences (all)	0	1	2
Peripheral swelling			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 49 (4.08%)
occurrences (all)	3	1	2
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)	5 / 52 (9.62%)	11 / 49 (22.45%)
occurrences (all)	2	6	17
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 9 (33.33%)	6 / 52 (11.54%)	11 / 49 (22.45%)
occurrences (all)	4	6	13
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	6 / 49 (12.24%)
occurrences (all)	1	1	6
Lung consolidation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	2 / 49 (4.08%)
occurrences (all)	0	1	3
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	3 / 49 (6.12%)
occurrences (all)	1	1	3
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)	3 / 52 (5.77%)	0 / 49 (0.00%)
occurrences (all)	0	3	0
Productive cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	2 / 49 (4.08%)
occurrences (all)	0	1	4
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences (all)	1	1	1
Hallucination			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 9 (33.33%)	1 / 52 (1.92%)	5 / 49 (10.20%)
occurrences (all)	3	1	5
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	4 / 49 (8.16%)
occurrences (all)	0	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	2 / 49 (4.08%)
occurrences (all)	2	0	2
Blood creatinine increased			

subjects affected / exposed	0 / 9 (0.00%)	3 / 52 (5.77%)	2 / 49 (4.08%)
occurrences (all)	0	3	2
Gamma−glutamyltransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	4 / 49 (8.16%)
occurrences (all)	0	8	4
Weight decreased			
subjects affected / exposed	1 / 9 (11.11%)	4 / 52 (7.69%)	8 / 49 (16.33%)
occurrences (all)	1	4	8
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	3 / 52 (5.77%)	2 / 49 (4.08%)
occurrences (all)	0	3	2
White blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	5 / 49 (10.20%)
occurrences (all)	0	1	7
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 9 (22.22%)	17 / 52 (32.69%)	9 / 49 (18.37%)
occurrences (all)	3	18	12
Laceration			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Limb injury			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 9 (11.11%)	2 / 52 (3.85%)	2 / 49 (4.08%)
occurrences (all)	1	2	5
Palpitations			
subjects affected / exposed	2 / 9 (22.22%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Sinus tachycardia			

subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	3 / 49 (6.12%)
occurrences (all)	0	2	4
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	3 / 49 (6.12%)
occurrences (all)	0	1	3
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)	4 / 52 (7.69%)	8 / 49 (16.33%)
occurrences (all)	1	5	8
Dysgeusia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 52 (5.77%)	3 / 49 (6.12%)
occurrences (all)	0	3	3
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Presyncope			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	3 / 9 (33.33%)	5 / 52 (9.62%)	8 / 49 (16.33%)
occurrences (all)	4	7	11
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 9 (33.33%)	3 / 52 (5.77%)	18 / 49 (36.73%)
occurrences (all)	3	3	25
Leukopenia			
subjects affected / exposed	2 / 9 (22.22%)	4 / 52 (7.69%)	8 / 49 (16.33%)
occurrences (all)	2	7	11
Neutropenia			
subjects affected / exposed	5 / 9 (55.56%)	12 / 52 (23.08%)	30 / 49 (61.22%)
occurrences (all)	12	34	94
Thrombocytopenia			

subjects affected / exposed	3 / 9 (33.33%)	7 / 52 (13.46%)	28 / 49 (57.14%)
occurrences (all)	15	9	70
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	1 / 49 (2.04%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)	5 / 52 (9.62%)	0 / 49 (0.00%)
occurrences (all)	0	5	0
Abdominal pain			
subjects affected / exposed	2 / 9 (22.22%)	6 / 52 (11.54%)	5 / 49 (10.20%)
occurrences (all)	3	7	7
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)	2 / 52 (3.85%)	3 / 49 (6.12%)
occurrences (all)	1	2	3
Constipation			
subjects affected / exposed	3 / 9 (33.33%)	5 / 52 (9.62%)	10 / 49 (20.41%)
occurrences (all)	4	5	10
Diarrhoea			
subjects affected / exposed	5 / 9 (55.56%)	21 / 52 (40.38%)	24 / 49 (48.98%)
occurrences (all)	14	27	47
Dyspepsia			
subjects affected / exposed	2 / 9 (22.22%)	3 / 52 (5.77%)	0 / 49 (0.00%)
occurrences (all)	2	3	0
Dysphagia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 52 (5.77%)	1 / 49 (2.04%)
occurrences (all)	1	3	1
Large intestine polyp			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			

subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	3 / 49 (6.12%)
occurrences (all)	1	0	4
Nausea			
subjects affected / exposed	7 / 9 (77.78%)	14 / 52 (26.92%)	32 / 49 (65.31%)
occurrences (all)	12	16	58
Stomatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	5 / 49 (10.20%)
occurrences (all)	0	0	5
Vomiting			
subjects affected / exposed	4 / 9 (44.44%)	7 / 52 (13.46%)	23 / 49 (46.94%)
occurrences (all)	7	12	43
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	3 / 49 (6.12%)
occurrences (all)	1	1	3
Pruritus			
subjects affected / exposed	1 / 9 (11.11%)	3 / 52 (5.77%)	1 / 49 (2.04%)
occurrences (all)	2	3	1
Psoriasis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Skin lesion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Yellow skin			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 9 (22.22%)	0 / 52 (0.00%)	2 / 49 (4.08%)
occurrences (all)	2	0	2
Renal colic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 52 (5.77%)	5 / 49 (10.20%)
occurrences (all)	1	3	5
Back pain			
subjects affected / exposed	2 / 9 (22.22%)	2 / 52 (3.85%)	1 / 49 (2.04%)
occurrences (all)	2	2	1
Joint swelling			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	4 / 49 (8.16%)
occurrences (all)	0	2	6
Periarthritis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Aspergillus infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	4 / 49 (8.16%)
occurrences (all)	0	2	4
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences (all)	1	2	0
Conjunctivitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 49 (4.08%)
occurrences (all)	1	1	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Lung infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	4 / 49 (8.16%)
occurrences (all)	0	0	4
Mycobacterium kansasii infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	4 / 49 (8.16%)
occurrences (all)	1	0	6
Oral herpes			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	6
Perineal abscess			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	3 / 52 (5.77%)	3 / 49 (6.12%)
occurrences (all)	1	3	5
Upper respiratory tract infection			
subjects affected / exposed	2 / 9 (22.22%)	6 / 52 (11.54%)	6 / 49 (12.24%)
occurrences (all)	2	9	8
Urinary tract infection			

subjects affected / exposed	1 / 9 (11.11%)	4 / 52 (7.69%)	4 / 49 (8.16%)
occurrences (all)	1	4	9
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 9 (22.22%)	3 / 52 (5.77%)	1 / 49 (2.04%)
occurrences (all)	2	3	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	5 / 52 (9.62%)	10 / 49 (20.41%)
occurrences (all)	0	6	13
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)	6 / 52 (11.54%)	11 / 49 (22.45%)
occurrences (all)	2	7	16
Hypomagnesaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	5 / 49 (10.20%)
occurrences (all)	0	1	5
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Hypophosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 52 (5.77%)	5 / 49 (10.20%)
occurrences (all)	0	4	6

Non-serious adverse events	Chemotherapy-Containing Cohort: Arm C (BR)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Hypotension			

subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Orthostatic hypotension			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	5		
Catheter site pain			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	14 / 50 (28.00%)		
occurrences (all)	21		
Influenza like illness			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Mass			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Peripheral swelling			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Pyrexia			

subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 50 (22.00%)		
occurrences (all)	15		
Dyspnoea			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	3		
Lung consolidation			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	8		
Rhinorrhoea			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	5		
Throat irritation			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Hallucination			

subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	6		
Blood creatinine increased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Gamma−glutamyltransferase increased			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	8		
Neutrophil count decreased			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	12		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	6 / 50 (12.00%)		
occurrences (all)	6		
Laceration			

subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Headache			

subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	5		
Leukopenia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	17 / 50 (34.00%)		
occurrences (all)	57		
Thrombocytopenia			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	15		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	17 / 50 (34.00%)		
occurrences (all)	19		
Diarrhoea			

subjects affected / exposed	13 / 50 (26.00%)		
occurrences (all)	18		
Dyspepsia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Dysphagia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Large intestine polyp			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	22 / 50 (44.00%)		
occurrences (all)	34		
Stomatitis			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	13 / 50 (26.00%)		
occurrences (all)	18		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	6		
Psoriasis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		

Yellow skin			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Renal colic			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	7 / 50 (14.00%)		
occurrences (all)	8		
Joint swelling			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Periarthritis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		

Aspergillus infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	4 / 50 (8.00%)			
occurrences (all)	5			
Herpes zoster				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences (all)	1			
Lower respiratory tract infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Lung infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Mycobacterium kansasii infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	2 / 50 (4.00%)			
occurrences (all)	2			
Oral herpes				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences (all)	2			
Perineal abscess				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences (all)	0			

Rhinitis subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 5		
Sinusitis subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 4		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2014	The protocol was amended to clarify instructions for detection and reporting of liver function abnormalities; and for addition of EudraCT number 2014-000576-26.
25 April 2014	The protocol was amended to allow investigator's choice of a Chemotherapy Free Cohort or a Chemotherapy-Containing Regimen. Participants assigned to the Chemotherapy-Containing Cohort were subsequently randomized to standard chemo-immunotherapy (bendamustine + rituximab, BR) versus BR + venetoclax. This change was made in response to concerns that participants who required a rapid response to treatment should not be randomized to an unproven Chemotherapy Free regimen; Rituximab dosing regimen in Arm A (Chemotherapy-Free cohort) was modified to align more closely with published data. The revised regimen was: Rituximab 375 mg/m^2 on Cycle 1 on Days 1, 8, 15, and 22, followed by 5 additional doses of rituximab administered every 8 weeks on Day 1 of Cycles 4, 6, 8, 10, and 12.
06 January 2015	The standard lymphoma response criteria were updated; Participants with prior exposure to hepatitis B, as manifest by hepatitis B virus (HBV) serologies showing hepatitis B core antibody−positive and hepatitis B surface antigen−negative were previously excluded from the study; It was clarified that non-vasectomized males must practice birth control and refrain from sperm donation for 6 months after the last dose of rituximab; The rationale for sample size determination was clarified; It was clarified how the tissue punch was to be obtained for tissue microarrays; The Year 1 assessment could now be performed up to 4 weeks, instead of 2 weeks, to allow flexibility on the timing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported