Clinical trial results:
A phase 2 study of brentuximab vedotin in combination with standard of care treatment (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone [RCHOP]) or RCHP (rituximab, cyclophosphamide, doxorubicin, and prednisone) as front-line therapy in patients with diffuse large B-cell lymphoma (DLBCL)

Summary

EudraCT number	2015-004741-54
Trial protocol	CZ ES IT
Global end of trial date	01 May 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2018
First version publication date	13 May 2018

Trial information

Trial identification

Sponsor protocol code	SGN35-017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01925612
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seattle Genetics, Inc
Sponsor organisation address	21823 30th Dr SE, Bothell, United States, 98021-3907
Public contact	Chief Medical Officer, Seattle Genetics, Inc, 001 855-473-2436, medinfo@seagen.com
Scientific contact	Chief Medical Officer, Seattle Genetics, Inc, 001 855-473-2436, medinfo@seagen.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	Final
Date of interim/final analysis	15 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 May 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the antitumor activity of brentuximab vedotin administered in combination with RCHOP or RCHP, and in combination with RCHP versus RCHOP alone, as measured by the CR rate at the end of treatment per investigator assessment in treatment-naive patients with high-intermediate or high risk systemic DLBCL

To assess the safety profile of brentuximab vedotin administered at dose levels of 1.2 mg/kg versus 1.8 mg/kg in combination with RCHOP or brentuximab vedotin 1.8 mg/kg in combination with RCHP in treatment-naive patients with high-intermediate or high risk systemic DLBCL

Protection of trial subjects:

The protocol for this study was designed in accordance with the general ethical principles outlined in the Declaration of Helsinki. The conduct of all aspects of the study, including methods for obtaining informed consent, were also in accordance with principles enunciated in the declaration, the International Conference on Harmonisation (ICH) Good Clinical Practices (GCP), and applicable Food and Drug Administration (FDA) regulations/guidelines set forth in Title 21 CFR Parts 11, 50, 54, 56, and 312. The consent form approved by each IRB/IEC included all elements required by the applicable regional laws and regulations, including a statement that Seattle Genetics, Inc. and authorities had access to patient records. Consent was obtained from all patients before any protocol-required procedures were performed, including any procedure not part of normal patient care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2013
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	Poland: 2
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 80
Worldwide total number of subjects	85
EEA total number of subjects	5

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	39
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 30-Aug-2013 through 28-Nov-2016.

Pre-assignment

Screening details:

The population to be studied includes treatment-naive patients with systemic de novo or transformed DLBCL or follicular non-Hodgkin lymphoma (NHL) grade 3b.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Part 1 was randomized and open-label.
Part 2 was non-randomized and open-label.
Part 3 was randomized and open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: BV (1.2 mg/kg) + RCHOP

Arm description:

Part 1 of the study is randomized and open-label. Brentuximab vedotin was administered at 1.2mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).

Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	Adcetris, SGN-35
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.2mg/kg every 3 weeks by IV infusion

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

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

Dosage and administration details:

750 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.4 mg/m2 every 3 weeks by IV infusion for up to 6 cycles (dose capped at 2 mg total).

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg on Days 1 to 5 of each 3-week cycle, orally for up to 6 cycles.

Arm title	Part 1: BV (1.8 mg/kg) + RCHOP

Arm description:

Part 1 of the study is a randomized and open-label. Brentuximab vedotin was administered at 1.8 mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).

Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	Adcetris, SGN-35
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.8mg/kg every 3 weeks by IV infusion

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

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

Dosage and administration details:

750 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.4 mg/m2 every 3 weeks by IV infusion for up to 6 cycles (dose capped at 2 mg total).

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg on Days 1 to 5 of each 3-week cycle, orally for up to 6 cycles.

Arm title	Part 2: BV (1.8 mg/kg) + RCHP

Arm description:

Part 2 of the study was non-randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy (rituximab, cyclophosphamide, doxorubicin, and prednisone).

Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	Adcetris, SGN-35
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.8mg/kg every 3 weeks by IV infusion

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

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

Dosage and administration details:

750 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

100 mg on Days 1 to 5 of each 3-week cycle, orally for up to 6 cycles.

Arm title	Part 3: BV (1.8 mg/kg) + RCHP

Arm description:

Part 3 of the study was randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy.

Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	Adcetris, SGN-35
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.8mg/kg every 3 weeks by IV infusion

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

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

Dosage and administration details:

750 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg on Days 1 to 5 of each 3-week cycle, orally for up to 6 cycles.

Arm title	Part 3: RCHOP

Arm description:

Part 3 of the study was randomized and open-label. RCHOP chemotherapy was administered alone.

Arm type	Active comparator

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

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

Dosage and administration details:

750 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 every 3 weeks by IV infusion for up to 6 cycles.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.4 mg/m2 every 3 weeks by IV infusion for up to 6 cycles (dose capped at 2 mg total).

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg on Days 1 to 5 of each 3-week cycle, orally for up to 6 cycles.

Number of subjects in period 1	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP
Started	29	22	11
Completed	25	18	10
Not completed	4	4	1
Adverse event, serious fatal	1	1	-
Adverse event, non-fatal	2	2	-
Progressive Disease	1	1	1

Number of subjects in period 1	Part 3: BV (1.8 mg/kg) + RCHP	Part 3: RCHOP
Started	11	12

Completed	10	10
Not completed	1	2
Adverse event, serious fatal	1	2
Adverse event, non-fatal	-	-
Progressive Disease	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: BV (1.2 mg/kg) + RCHOP
Reporting group description:	
Part 1 of the study is randomized and open-label. Brentuximab vedotin was administered at 1.2mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).	
Reporting group title	Part 1: BV (1.8 mg/kg) + RCHOP
Reporting group description:	
Part 1 of the study is a randomized and open-label. Brentuximab vedotin was administered at 1.8 mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).	
Reporting group title	Part 2: BV (1.8 mg/kg) + RCHP
Reporting group description:	
Part 2 of the study was non-randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy (rituximab, cyclophosphamide, doxorubicin, and prednisone).	
Reporting group title	Part 3: BV (1.8 mg/kg) + RCHP
Reporting group description:	
Part 3 of the study was randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy.	
Reporting group title	Part 3: RCHOP
Reporting group description:	
Part 3 of the study was randomized and open-label. RCHOP chemotherapy was administered alone.	

Reporting group values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP
Number of subjects	29	22	11
Age categorical Units: Subjects			
Adults (18-64 years)	10	11	7
65 years and over	19	11	4
Age continuous Units: years			
median	70	64	59
full range (min-max)	33 to 80	21 to 81	22 to 78
Gender categorical Units: Subjects			
Female	13	6	4
Male	16	16	7
Ethnicity			
NIH/OMB			
Units: Subjects			
Hispanic or Latino	4	2	1
Not Hispanic or Latino	25	18	8
Unknown or Not Reported	0	2	2
Race			
NIH/OMB			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	1
White	27	17	8
More than one race	0	0	0
Unknown or Not Reported	1	3	1
Region of Enrollment			
Units: Subjects			
United States	29	22	11
Czechia	0	0	0
Poland	0	0	0
Italy	0	0	0
ECOG Performance Status			
Units: Subjects			
Zero	5	4	1
One	16	12	4
Two	8	6	6

Reporting group values	Part 3: BV (1.8 mg/kg) + RCHP	Part 3: RCHOP	Total
Number of subjects	11	12	85
Age categorical			
Units: Subjects			
Adults (18-64 years)	5	6	39
65 years and over	6	6	46
Age continuous			
Units: years			
median	68	65	
full range (min-max)	46 to 74	41 to 80	-
Gender categorical			
Units: Subjects			
Female	10	6	39
Male	1	6	46
Ethnicity			
NIH/OMB			
Units: Subjects			
Hispanic or Latino	0	1	8
Not Hispanic or Latino	11	11	73
Unknown or Not Reported	0	0	4
Race			
NIH/OMB			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	4
White	10	12	74
More than one race	0	0	0
Unknown or Not Reported	0	0	5
Region of Enrollment			
Units: Subjects			

United States	8	10	80
Czechia	1	1	2
Poland	2	0	2
Italy	0	1	1
ECOG Performance Status Units: Subjects			
Zero	4	4	18
One	4	3	39
Two	3	5	28

End points

End points reporting groups

Reporting group title	Part 1: BV (1.2 mg/kg) + RCHOP
Reporting group description:	
Part 1 of the study is randomized and open-label. Brentuximab vedotin was administered at 1.2mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).	
Reporting group title	Part 1: BV (1.8 mg/kg) + RCHOP
Reporting group description:	
Part 1 of the study is a randomized and open-label. Brentuximab vedotin was administered at 1.8 mg/kg in combination with standard RCHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).	
Reporting group title	Part 2: BV (1.8 mg/kg) + RCHP
Reporting group description:	
Part 2 of the study was non-randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy (rituximab, cyclophosphamide, doxorubicin, and prednisone).	
Reporting group title	Part 3: BV (1.8 mg/kg) + RCHP
Reporting group description:	
Part 3 of the study was randomized and open-label. Brentuximab vedotin (1.8 mg/kg) was administered in combination with RCHP chemotherapy.	
Reporting group title	Part 3: RCHOP
Reporting group description:	
Part 3 of the study was randomized and open-label. RCHOP chemotherapy was administered alone.	

Primary: Complete Remission Rate

End point title	Complete Remission Rate[1]
End point description:	
Number (count) of participants that achieved complete remission according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2007).	
End point type	Primary
End point timeframe:	
Up to 6 months	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Within-group analysis	

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Count of Participants	20	16	9	6

End point values	Part 3: RCHOP			
Subject group type	Reporting group			
Number of subjects analysed	12			

Units: Count of Participants	8			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Adverse Events

End point title	Incidence of Adverse Events[2]

End point description:

Number (count) of participants that experienced at least 1 adverse event.

End point type	Primary

End point timeframe:

Up to 6 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data for this end point were summarized per protocol.

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Count of Participants	29	22	11	11

End point values	Part 3: RCHOP			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Count of Participants	12			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Laboratory Abnormalities

End point title	Incidence of Laboratory Abnormalities[3]

End point description:

Number (count) of participants that experienced a Grade 3 or higher maximum post-baseline laboratory toxicity (hematology and chemistry)

End point type	Primary

End point timeframe:

Up to 6 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data for this end point were summarized per protocol.

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Count of Participants				
Any Hematology Test	10	16	4	6
Lymphocytes (x10^3/uL)	8	15	3	4
Absolute Neutrophil Count (x10^3/uL)	4	4	1	2
Neutrophils (x10^3/uL)	4	4	1	2
Leukocytes (x10^3/uL)	3	2	1	1
Hemoglobin (x10^3/uL)	0	1	0	1
Platelets (x10^3/uL)	1	1	0	0
Any Chemistry Test	4	7	2	1
Glucose (mg/dL)	3	5	0	0
Potassium (mEq)/L	0	2	1	1
Calcium (mg/dL)	1	1	0	0
Sodium (mEq/L)	0	2	0	0
Alanine Aminotransferase (IU/L)	0	0	1	0

End point values	Part 3: RCHOP			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Count of Participants				
Any Hematology Test	4			
Lymphocytes (x10^3/uL)	4			
Absolute Neutrophil Count (x10^3/uL)	0			
Neutrophils (x10^3/uL)	0			
Leukocytes (x10^3/uL)	1			
Hemoglobin (x10^3/uL)	0			
Platelets (x10^3/uL)	0			
Any Chemistry Test	3			
Glucose (mg/dL)	1			
Potassium (mEq)/L	2			
Calcium (mg/dL)	0			
Sodium (mEq/L)	0			
Alanine Aminotransferase (IU/L)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

Number (count) of participants that achieved complete or partial remission at the end of treatment according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2007).

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Count of Participants	23	19	10	10

End point values	Part 3: RCHOP			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Count of Participants	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival

End point title	Progression-free Survival

End point description:

Median progression-free survival (in months) and observed minimum-maximum range.

Insufficient data to determine median value in all arms. Arms and full ranges listed below:
Part 1: BV (1.2 mg/kg) + RCHOP (0.62, 40.21+)
Part 1: BV (1.8mg/kg) + RCHOP (1.28, 39.85+)
Part 2: BV (1.8 mg/kg) + RCHP (3.35, 24.34+)
Part 3: BV (1.8 mg/kg) + RCHP (3.25, 15.41+)
Part 3: RCHOP (1.25, 16.43+)

End point type	Secondary

End point timeframe:

Up to approximately 4 years

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Months				
median (full range (min-max))	999 (0.62 to 999)	999 (1.28 to 999)	999 (3.35 to 999)	999 (3.25 to 999)

End point values	Part 3: RCHOP			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Months				
median (full range (min-max))	999 (1.25 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Median progression-free survival (in months) and observed minimum-maximum range.

Insufficient data to calculate median for 3 arms. Arms and full ranges are listed here:
Part 1: BV (1.2 mg/kg) + RCHOP (0.62, 42.79)
Part 2: BV (1.8 mg/kg) + RCHP (16.56, 25.76)
Part 3: BV (1.8 mg/kg) + RCHP (3.25, 16.85)

End point type	Secondary

End point timeframe:

Up to approximately 4 years

End point values	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP	Part 3: BV (1.8 mg/kg) + RCHP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	22	11	11
Units: Months				
median (full range (min-max))	999 (0.62 to 999)	18.1 (1.28 to 44.29)	999 (16.56 to 999)	999 (3.25 to 999)

End point values	Part 3: RCHOP			

Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Months				
median (full range (min-max))	4.6 (1.25 to 19.22)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from study Day 1 (predose) though the EOT visit or 30 days after the last study treatment (mono- or combination therapy), whichever was later. However, all protocol-related AEs were collected from the time of informed consent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Part 1: BV (1.2 mg/kg) + RCHOP
Reporting group description: -	
Reporting group title	Part 1: BV (1.8 mg/kg) + RCHOP
Reporting group description: -	
Reporting group title	Part 2: BV (1.8 mg/kg) + RCHP
Reporting group description: -	
Reporting group title	Part 3: BV (1.8 mg/kg) + RCHP
Reporting group description: -	
Reporting group title	Part 3: RCHOP
Reporting group description: -	

Serious adverse events	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 29 (55.17%)	14 / 22 (63.64%)	5 / 11 (45.45%)
number of deaths (all causes)	6	7	1
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer metastatic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myelodysplastic syndrome			

subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Chest pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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 failure			

subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (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			
Neutrophil count decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Cytomegalovirus test positive			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Platelet count decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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 arrest			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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 congestive			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Left ventricular dysfunction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Guillain-Barre syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Seizure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	8 / 29 (27.59%)	8 / 22 (36.36%)	2 / 11 (18.18%)
occurrences causally related to treatment / all	10 / 13	9 / 13	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Pancytopenia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Skin and subcutaneous tissue disorders			
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (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 and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Renal failure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (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
Infections and infestations			
Bacteraemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (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
Sepsis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Bronchiolitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (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
Escherichia infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pantoea agglomerans infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 3: BV (1.8 mg/kg) + RCHP	Part 3: RCHOP	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	4 / 12 (33.33%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer metastatic			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus test positive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pantoea agglomerans infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: BV (1.2 mg/kg) + RCHOP	Part 1: BV (1.8 mg/kg) + RCHOP	Part 2: BV (1.8 mg/kg) + RCHP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)	22 / 22 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
Hypotension			
subjects affected / exposed	1 / 29 (3.45%)	6 / 22 (27.27%)	0 / 11 (0.00%)
occurrences (all)	1	9	0
Flushing			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Hot flush			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	4 / 29 (13.79%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 29 (58.62%)	16 / 22 (72.73%)	7 / 11 (63.64%)
occurrences (all)	28	30	7
Asthenia			

subjects affected / exposed	8 / 29 (27.59%)	7 / 22 (31.82%)	0 / 11 (0.00%)
occurrences (all)	19	8	0
Chills			
subjects affected / exposed	7 / 29 (24.14%)	4 / 22 (18.18%)	3 / 11 (27.27%)
occurrences (all)	12	4	3
Oedema peripheral			
subjects affected / exposed	7 / 29 (24.14%)	7 / 22 (31.82%)	1 / 11 (9.09%)
occurrences (all)	9	8	2
Pyrexia			
subjects affected / exposed	6 / 29 (20.69%)	6 / 22 (27.27%)	1 / 11 (9.09%)
occurrences (all)	9	6	1
Mucosal inflammation			
subjects affected / exposed	2 / 29 (6.90%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	4	3	0
Influenza like illness			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Peripheral swelling			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	3	2	0
Malaise			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	4 / 11 (36.36%)
occurrences (all)	2	0	4
Dyspnoea			
subjects affected / exposed	7 / 29 (24.14%)	9 / 22 (40.91%)	0 / 11 (0.00%)
occurrences (all)	7	12	0
Cough			

subjects affected / exposed	3 / 29 (10.34%)	4 / 22 (18.18%)	1 / 11 (9.09%)
occurrences (all)	3	7	1
Nasal congestion			
subjects affected / exposed	3 / 29 (10.34%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Oropharyngeal pain			
subjects affected / exposed	4 / 29 (13.79%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	4	1	0
Respiratory tract irritation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	3 / 29 (10.34%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Sinus congestion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Upper-airway cough syndrome			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Pleural effusion			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	3	2	0
Dysphonia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Hiccups			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 29 (24.14%)	8 / 22 (36.36%)	2 / 11 (18.18%)
occurrences (all)	7	8	2

Anxiety			
subjects affected / exposed	3 / 29 (10.34%)	4 / 22 (18.18%)	0 / 11 (0.00%)
occurrences (all)	3	5	0
Confusional state			
subjects affected / exposed	4 / 29 (13.79%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	4	2	0
Depression			
subjects affected / exposed	3 / 29 (10.34%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Investigations			
Weight decreased			
subjects affected / exposed	10 / 29 (34.48%)	8 / 22 (36.36%)	1 / 11 (9.09%)
occurrences (all)	16	13	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
International normalised ratio increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 29 (13.79%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	5	1	0
Contusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1

Cardiac disorders			
Tachycardia			
subjects affected / exposed	8 / 29 (27.59%)	4 / 22 (18.18%)	0 / 11 (0.00%)
occurrences (all)	9	4	0
Palpitations			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Atrial fibrillation			
subjects affected / exposed	1 / 29 (3.45%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	1	5	0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	16 / 29 (55.17%)	15 / 22 (68.18%)	6 / 11 (54.55%)
occurrences (all)	25	27	6
Headache			
subjects affected / exposed	6 / 29 (20.69%)	6 / 22 (27.27%)	3 / 11 (27.27%)
occurrences (all)	7	6	5
Dizziness			
subjects affected / exposed	4 / 29 (13.79%)	8 / 22 (36.36%)	1 / 11 (9.09%)
occurrences (all)	6	9	1
Peripheral motor neuropathy			
subjects affected / exposed	4 / 29 (13.79%)	8 / 22 (36.36%)	0 / 11 (0.00%)
occurrences (all)	11	14	0
Dysgeusia			
subjects affected / exposed	4 / 29 (13.79%)	5 / 22 (22.73%)	2 / 11 (18.18%)
occurrences (all)	6	5	2
Restless legs syndrome			
subjects affected / exposed	3 / 29 (10.34%)	0 / 22 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	2
Balance disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Syncope			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			

subjects affected / exposed	3 / 29 (10.34%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			
subjects affected / exposed	3 / 29 (10.34%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	10 / 29 (34.48%)	7 / 22 (31.82%)	4 / 11 (36.36%)
occurrences (all)	27	20	5
Anaemia			
subjects affected / exposed	9 / 29 (31.03%)	7 / 22 (31.82%)	2 / 11 (18.18%)
occurrences (all)	26	20	5
Thrombocytopenia			
subjects affected / exposed	5 / 29 (17.24%)	3 / 22 (13.64%)	2 / 11 (18.18%)
occurrences (all)	20	19	2
Leukopenia			
subjects affected / exposed	2 / 29 (6.90%)	4 / 22 (18.18%)	0 / 11 (0.00%)
occurrences (all)	13	16	0
Febrile neutropenia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 29 (10.34%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	3	2	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	1 / 29 (3.45%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	1	4	0
Vision blurred			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	14 / 29 (48.28%)	15 / 22 (68.18%)	8 / 11 (72.73%)
occurrences (all)	24	23	9
Diarrhoea			

subjects affected / exposed	14 / 29 (48.28%)	15 / 22 (68.18%)	3 / 11 (27.27%)
occurrences (all)	19	23	4
Constipation			
subjects affected / exposed	8 / 29 (27.59%)	9 / 22 (40.91%)	6 / 11 (54.55%)
occurrences (all)	9	12	6
Vomiting			
subjects affected / exposed	7 / 29 (24.14%)	14 / 22 (63.64%)	2 / 11 (18.18%)
occurrences (all)	9	17	2
Stomatitis			
subjects affected / exposed	8 / 29 (27.59%)	3 / 22 (13.64%)	3 / 11 (27.27%)
occurrences (all)	10	4	3
Abdominal pain			
subjects affected / exposed	6 / 29 (20.69%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	6	3	0
Flatulence			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Haemorrhoids			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	2 / 11 (18.18%)
occurrences (all)	2	1	2
Oral pain			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	2 / 11 (18.18%)
occurrences (all)	1	2	2
Dyspepsia			
subjects affected / exposed	4 / 29 (13.79%)	3 / 22 (13.64%)	1 / 11 (9.09%)
occurrences (all)	5	3	2
Dry mouth			
subjects affected / exposed	3 / 29 (10.34%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	3	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 29 (6.90%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	2	3	0
Dysphagia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Epigastric discomfort			

subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Tongue discolouration			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Toothache			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 29 (17.24%)	9 / 22 (40.91%)	8 / 11 (72.73%)
occurrences (all)	6	10	10
Dry skin			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	2 / 11 (18.18%)
occurrences (all)	2	2	2
Night sweats			
subjects affected / exposed	4 / 29 (13.79%)	2 / 22 (9.09%)	2 / 11 (18.18%)
occurrences (all)	4	2	2
Skin hyperpigmentation			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	2
Pruritus			
subjects affected / exposed	1 / 29 (3.45%)	3 / 22 (13.64%)	1 / 11 (9.09%)
occurrences (all)	3	3	2
Blister			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	2 / 29 (6.90%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Urticaria			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Hyperhidrosis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Pollakiuria			
subjects affected / exposed	3 / 29 (10.34%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 29 (17.24%)	4 / 22 (18.18%)	1 / 11 (9.09%)
occurrences (all)	6	4	1
Muscle spasms			
subjects affected / exposed	6 / 29 (20.69%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	7	2	0
Myalgia			
subjects affected / exposed	4 / 29 (13.79%)	4 / 22 (18.18%)	0 / 11 (0.00%)
occurrences (all)	5	7	0
Back pain			
subjects affected / exposed	5 / 29 (17.24%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	5	2	0
Bone pain			
subjects affected / exposed	3 / 29 (10.34%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	3	3	0
Flank pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	2	2	1
Pain in extremity			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Muscular weakness			

subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Candida infection			
subjects affected / exposed	5 / 29 (17.24%)	5 / 22 (22.73%)	2 / 11 (18.18%)
occurrences (all)	8	7	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)	1 / 22 (4.55%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Oral candidiasis			
subjects affected / exposed	4 / 29 (13.79%)	2 / 22 (9.09%)	1 / 11 (9.09%)
occurrences (all)	4	2	1
Cellulitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	2
Fungal infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Herpes virus infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 22 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	3 / 29 (10.34%)	0 / 22 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Sinusitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 29 (24.14%)	10 / 22 (45.45%)	2 / 11 (18.18%)
occurrences (all)	10	15	2
Dehydration			

subjects affected / exposed	3 / 29 (10.34%)	9 / 22 (40.91%)	2 / 11 (18.18%)
occurrences (all)	3	11	3
Hypokalaemia			
subjects affected / exposed	6 / 29 (20.69%)	5 / 22 (22.73%)	1 / 11 (9.09%)
occurrences (all)	10	8	1
Hypomagnesaemia			
subjects affected / exposed	1 / 29 (3.45%)	5 / 22 (22.73%)	0 / 11 (0.00%)
occurrences (all)	1	8	0
Hypophosphataemia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 22 (9.09%)	1 / 11 (9.09%)
occurrences (all)	1	6	1
Hyperglycaemia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 22 (9.09%)	0 / 11 (0.00%)
occurrences (all)	4	2	0
Hyponatraemia			
subjects affected / exposed	1 / 29 (3.45%)	3 / 22 (13.64%)	0 / 11 (0.00%)
occurrences (all)	1	11	0

Non-serious adverse events	Part 3: BV (1.8 mg/kg) + RCHP	Part 3: RCHOP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	12 / 12 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Flushing			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)	3 / 12 (25.00%)	
occurrences (all)	2	4	
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Chills			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Mucosal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	3 / 11 (27.27%)	4 / 12 (33.33%)	
occurrences (all)	3	4	
Cough			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory tract irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Sinus congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Upper-airway cough syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hiccups			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 11 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
International normalised ratio increased			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
White blood cell count decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Contusion			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 11 (36.36%)	4 / 12 (33.33%)	
occurrences (all)	6	4	
Headache			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Dizziness			
subjects affected / exposed	2 / 11 (18.18%)	3 / 12 (25.00%)	
occurrences (all)	2	3	
Peripheral motor neuropathy			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Restless legs syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Balance disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 11 (36.36%)	2 / 12 (16.67%)	
occurrences (all)	4	4	
Anaemia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 12 (8.33%)	
occurrences (all)	8	1	
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Febrile neutropenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 11 (36.36%)	2 / 12 (16.67%)	
occurrences (all)	6	2	
Diarrhoea			
subjects affected / exposed	6 / 11 (54.55%)	1 / 12 (8.33%)	
occurrences (all)	8	1	
Constipation			
subjects affected / exposed	1 / 11 (9.09%)	5 / 12 (41.67%)	
occurrences (all)	1	5	
Vomiting			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Stomatitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oral pain			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Dysphagia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Epigastric discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Tongue discolouration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 11 (27.27%)	3 / 12 (25.00%)	
occurrences (all)	3	4	
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Skin hyperpigmentation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Blister			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Myalgia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Bone pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Muscular weakness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Oral candidiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Herpes virus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 11 (18.18%)	3 / 12 (25.00%)	
occurrences (all)	2	3	
Dehydration			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Hypokalaemia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 12 (16.67%)	
occurrences (all)	3	3	
Hypomagnesaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	2	2	
Hypophosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	4	
Hypoalbuminaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2013	• Removed CD30 expression by local pathology laboratory as a screening assessment, for operational ease. CD30 expression was still evaluated by central pathology laboratory. • Removed randomization stratification by CD30 expression because it was unlikely that significant imbalances would be observed between treatment arms. • Clarified that the optional malignant lymphoma biopsy may be requested for patients who progress at any time during their participation on the study. • Clarified the definition of PFS and associated censoring rules.
04 November 2013	• Clarified the permissible use of corticosteroids prior to first dose • Clarified that routine vaccination was permitted as long as the vaccine did not contain live microorganisms • Added serology for hepatitis B surface antigen and anti-hepatitis B core antibody to the screening assessments to ensure exclusion of patients who are positive for either hepatitis B surface antigen or anti-hepatitis B core antibody because of the risk of hepatitis B reactivation in patients treated with rituximab • Clarified the definition of study treatment-related AEs • Clarified that certain AEs may be followed until resolution, return to baseline, or study closure
26 February 2014	• Revised protocol to define high-intermediate and high risk patients based on standard IPI or age-adjusted IPI • Clarified to show that all samples provided by patients may be used to evaluate disease-related biomarkers, including baseline tumor specimens and not just those specimens taken on treatment
14 January 2015	• Added new part to the study (Part 2) to assess safety, efficacy, and PK of BV + RCHP; numerous sections of the protocol were updated
10 August 2015	• Added new part to the study (Part 3) to assess safety and antitumor activity of BV + RCHP versus RCHOP alone; numerous sections of the protocol were updated • Revised Inclusion criterion No. 7 to clarify patients must use 2 effective contraception methods during the study • Revised Exclusion criterion No. 12 to allow patients with negative PCR assay • Added instructions regarding testing for hepatitis B PCR assay and concomitant therapy with antiviral prophylaxis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported