Clinical trial results:
A Phase 1/2 Open-Label Study to Evaluate the Safety and Efficacy of Loncastuximab Tesirine and Ibrutinib in Patients with Advanced Diffuse Large B-Cell Lymphoma or Mantle Cell Lymphoma (LOTIS-3)

Summary

EudraCT number	2018-002625-38
Trial protocol	BE GB IT
Global end of trial date	08 November 2022

Results information

Result version number	v1 (current)
This version publication date	07 December 2023
First version publication date	07 December 2023

Trial information

Trial identification

Sponsor protocol code	ADCT-402-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03684694
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ADC Therapeutics SA
Sponsor organisation address	Route de la Corniche, 3B, Epalinges, Switzerland, 1066
Public contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com
Scientific contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.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	08 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1: To characterize the safety and tolerability of loncastuximab tesirine in combination with ibrutinib, and to identify the maximum tolerated dose (MTD) /recommended dose and schedule for future studies.
Phase 2: To evaluate the efficacy of loncastuximab tesirine in combination with ibrutinib in participants with relapsed or refractory diffuse large B-Cell lymphoma (DLBCL).

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP] guideline CPMP/ICH/135/95) and the European Union Clinical Trial Directive (EU CTD): Directive 2001/20/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	136
EEA total number of subjects	106

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)	43
From 65 to 84 years	93
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

136 participants were enrolled into sites in the United States, Belgium, France, Italy, and Spain.

Pre-assignment

Screening details:

Participants were screened for eligibility to enroll within 28 days prior to the start of treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib

Arm description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Arm title	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib

Arm description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab

tesirine given 4 weeks apart.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Arm title	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib

Arm description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Arm title	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL

Arm description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Arm title	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL

Arm description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Arm title	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL

Arm description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

Number of subjects in period 1	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib
Started	37	4	6
Completed	0	1	1
Not completed	37	3	5
Consent withdrawn by subject	1	-	-
Investigator/Sponsor Decision	12	2	1
Death	24	-	3
Miscellaneous	-	1	-
Lost to follow-up	-	-	1

Number of subjects in period 1	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL
Started	49	30	10
Completed	0	0	0
Not completed	49	30	10
Consent withdrawn by subject	-	-	1
Investigator/Sponsor Decision	17	16	6
Death	28	14	3
Miscellaneous	3	-	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL

Reporting group description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL

Reporting group description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL

Reporting group description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib
Number of subjects	37	4	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0

Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	1	3
From 65-84 years	23	3	3
85 years and over	3	0	0
Gender categorical Units: Subjects			
Female	10	2	2
Male	27	2	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	37	4	6
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
Asian	0	0	0
Black or African American	1	0	0
White	35	4	6
Unknown or Not Reported	1	0	0

Reporting group values	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL
Number of subjects	49	30	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	10	5
From 65-84 years	36	18	4
85 years and over	0	2	1
Gender categorical Units: Subjects			
Female	19	9	3
Male	30	21	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	0
Not Hispanic or Latino	47	27	9
Unknown or Not Reported	0	3	1
Race (NIH/OMB) Units: Subjects			

Asian	1	0	0
Black or African American	1	0	0
White	43	26	10
Unknown or Not Reported	4	4	0

Reporting group values	Total		
Number of subjects	136		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	43		
From 65-84 years	87		
85 years and over	6		
Gender categorical Units: Subjects			
Female	45		
Male	91		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	130		
Unknown or Not Reported	4		
Race (NIH/OMB) Units: Subjects			
Asian	1		
Black or African American	2		
White	124		
Unknown or Not Reported	9		

End points reporting groups

Reporting group title	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL

Reporting group description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL

Reporting group description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL

Reporting group description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Subject analysis set title	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Subject analysis set title	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Subject analysis set title	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Subject analysis set title	Phase 2: Non-GCB DLBCL
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Subject analysis set title	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Subject analysis set title	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

Primary: Phase 1: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Phase 1: Number of Participants With Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

A TEAE was defined as an adverse event (AE) that occurred or worsened in the period extending from the first dose of study drug to 30 days after the last dose of study drug in this study or start of a new anticancer therapy, whichever is earlier. Any clinically significant changes form baseline in safety laboratory values, vital signs, Eastern Cooperative Oncology Group (ECOG) performance status, and 12-lead electrocardiograms (ECGs) which occurred after first dose of study drug were recorded as TEAEs.

End point type	Primary

End point timeframe:

Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	4	6	
Units: participants	37	4	6	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Serious TEAEs

End point title	Phase 1: Number of Participants With Serious TEAEs[2]

End point description:

A serious TEAE was defined as any AE which occurred after the first dose of study drug that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization (hospitalization for elective procedures or for protocol compliance was not considered a serious adverse event), resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or important medical events that did not meet the preceding criteria but based on appropriate medical judgement may have jeopardized the participant or may have required medical or surgical intervention to prevent any of the outcomes listed above.

End point type	Primary

End point timeframe:

Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	4	6	
Units: participants	19	0	3	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose-Limiting Toxicities (DLTs)

End point title	Phase 1: Number of Participants With Dose-Limiting Toxicities (DLTs)[3]

End point description:

A DLT was defined as any of the following events which occur during the DLT Period (first 21 days of ibrutinib treatment), except those that are clearly due to underlying disease or extraneous causes: a hematologic DLT (grade ≥3 anaemia, grade 4/febrile neutropenia, grade ≥3 thrombocytopenia), a non-hematologic DLT (including aspartate aminotransferase [AST] and/or alanine aminotransferase [ALT] >3× upper limit of normal (ULN) and bilirubin >2× ULN), any other non-hematologic toxicities ≥ Grade 3, with exceptions.

End point type	Primary

End point timeframe:

21 days

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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	4	6	
Units: participants	0	0	2	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose Interruptions

End point title	Phase 1: Number of Participants With Dose Interruptions[4]

End point description:

Measured in the safety population, which included all participants who received study drug.

End point type	Primary

End point timeframe:

Up to a maximum of 686 days

Notes:

[4] - 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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	4	6	
Units: participants	1	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose Reductions

End point title	Phase 1: Number of Participants With Dose Reductions[5]

End point description:

Measured in the safety population, which included all participants who received study drug.

End point type	Primary

End point timeframe:

Up to a maximum of 686 days

Notes:

[5] - 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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	4	6	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Complete Response Rate (CRR)

End point title	Phase 2: Complete Response Rate (CRR)[6]

End point description:

CRR according to the 2014 Lugano classifications determined by Independent Review Committee (IRC). CRR was defined as the percentage of participants with a best overall response (BOR) of complete response (CR). Measured in the efficacy analysis set, which included all participants who received at least 1 dose of study drug, who had valid baseline disease assessment(s), and who had at least one valid post-baseline disease assessment. Participants who did not have a post-baseline assessment due to early clinical progression or death (after receiving study drug) were also included.

End point type	Primary

End point timeframe:

Up to approximately 38 months

Notes:

[6] - 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: No statistical analyses were pre-specified for this endpoint. Descriptive statistics are presented.

End point values	Phase 2: Non-GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	30	10	
Units: percentage of participants				
number (confidence interval 95%)	27.1 (15.3 to 41.8)	26.7 (12.3 to 45.9)	90.0 (55.5 to 99.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality from enrollment until approx. 4 years. For serious adverse events and other adverse events, from Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

Reporting group title	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL

Reporting group description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL

Reporting group description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Reporting group title	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL

Reporting group description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

Serious adverse events	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 37 (51.35%)	0 / 4 (0.00%)	3 / 6 (50.00%)
number of deaths (all causes)	24	0	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Lymphoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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 associated fever			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Hypotension			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Death			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Disease progression			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
General physical health deterioration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Oedema peripheral			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Dyspnoea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Haemoptysis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Lung disorder			

subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pleural effusion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pulmonary embolism			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Humerus fracture			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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 disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Coronary artery disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Pericardial disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Pericardial effusion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pericarditis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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

Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Lymph node pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Neutropenia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Abdominal pain upper			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Ascites			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Colitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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

Pneumatosis intestinalis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Stomatitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Vomiting			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
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 failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Bone swelling			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Campylobacter infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Citrobacter infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			

subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Folliculitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pneumonia fungal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Pneumonia parainfluenzae viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Pneumonia viral			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Urinary tract infection bacterial			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (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
Urosepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (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

Serious adverse events	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 49 (55.10%)	5 / 30 (16.67%)	5 / 10 (50.00%)

number of deaths (all causes)	28	14	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Lymphoma			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tumour associated fever			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Hypotension			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Death			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Disease progression			

subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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
General physical health deterioration			
subjects affected / exposed	4 / 49 (8.16%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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			
Acute pulmonary oedema			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Dyspnoea			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Haemoptysis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Lung disorder			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Pleural effusion			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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 embolism			

subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Respiratory failure			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Humerus fracture			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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 disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Cardiomyopathy			

subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Cardiopulmonary failure			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial disease			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Pericardial effusion			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Pericarditis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic disorder			

subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Lymph node pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Neutropenia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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 disorders			
Abdominal pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Abdominal pain upper			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Ascites			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Colitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Pneumatosis intestinalis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Stomatitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Vomiting			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
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			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
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 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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
Haematuria			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Renal failure			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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

Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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
Musculoskeletal and connective tissue disorders			
Bone swelling			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (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
Campylobacter infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Citrobacter infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Corona virus infection			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Enterococcal infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Escherichia sepsis			

subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Folliculitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Pneumocystis jirovecii infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Pneumonia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Pneumonia fungal			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Pneumonia viral			
subjects affected / exposed	5 / 49 (10.20%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 1
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (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
Urosepsis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (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
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (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

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

Non-serious adverse events	Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib	Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 37 (100.00%)	4 / 4 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Hypertension			

subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Phlebitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 37 (16.22%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Chest pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Early satiety			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	9 / 37 (24.32%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	10	0	3
Generalised oedema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Mucosal inflammation			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	6 / 37 (16.22%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	10	2	1
Pain			

subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	3
Sensation of foreign body			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 37 (16.22%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	9	1	0
Dry throat			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Epistaxis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Confusional state			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	9	0	5
Amylase increased			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 37 (5.41%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	3	1	3
Blood bilirubin increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Blood iron decreased			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Coronavirus test positive			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	11	0	3
Lipase increased			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Weight decreased			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Weight increased			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	1 / 37 (2.70%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Limb injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Bradycardia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Sinus bradycardia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 37 (2.70%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	2 / 37 (5.41%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Neuropathy peripheral			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 37 (24.32%)	2 / 4 (50.00%)	4 / 6 (66.67%)
occurrences (all)	14	4	8
Leukopenia			

subjects affected / exposed	2 / 37 (5.41%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	3	4	1
Lymphadenopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	5 / 37 (13.51%)	3 / 4 (75.00%)	1 / 6 (16.67%)
occurrences (all)	26	4	3
Thrombocytopenia			
subjects affected / exposed	17 / 37 (45.95%)	2 / 4 (50.00%)	4 / 6 (66.67%)
occurrences (all)	38	3	8
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 37 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	2
Abdominal pain upper			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Diarrhoea			
subjects affected / exposed	9 / 37 (24.32%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	13	2	1
Dry mouth			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	2
Dysphagia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Faeces soft			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Gastritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	9 / 37 (24.32%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	9	1	1
Odynophagia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pancreatitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			

subjects affected / exposed	1 / 37 (2.70%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cholecystocholangitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatocellular injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood blister			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis bullous			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Dry skin			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Ecchymosis			

subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	2 / 37 (5.41%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Lividity			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Macule			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Onychoclasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Palmar erythema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Photosensitivity reaction			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Pruritus			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Purpura			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	7 / 37 (18.92%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	12	1	2
Rash macular			

subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash vesicular			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Back pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Muscle spasms			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	6 / 37 (16.22%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Corona virus infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Genital infection fungal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 37 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Oral fungal infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Oral herpes			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Rhinitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 37 (13.51%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Hypercalcaemia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Hyperglycaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Hypermagnesaemia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	8	0	0
Hypokalaemia			
subjects affected / exposed	6 / 37 (16.22%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	8	1	1
Hypomagnesaemia			
subjects affected / exposed	5 / 37 (13.51%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Hyponatraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	4 / 37 (10.81%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 37 (5.41%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Phase 2: Non-Germinal Center B-cell (GCB) DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL	Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 49 (97.96%)	30 / 30 (100.00%)	10 / 10 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Haematoma			

subjects affected / exposed	1 / 49 (2.04%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	2	3	0
Hypertension			
subjects affected / exposed	2 / 49 (4.08%)	1 / 30 (3.33%)	3 / 10 (30.00%)
occurrences (all)	2	2	3
Phlebitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 49 (10.20%)	2 / 30 (6.67%)	3 / 10 (30.00%)
occurrences (all)	8	2	4
Chest pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	14 / 49 (28.57%)	2 / 30 (6.67%)	3 / 10 (30.00%)
occurrences (all)	20	3	3
Generalised oedema			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			

subjects affected / exposed	12 / 49 (24.49%)	3 / 30 (10.00%)	1 / 10 (10.00%)
occurrences (all)	16	3	1
Pain			
subjects affected / exposed	2 / 49 (4.08%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	2	2	0
Peripheral swelling			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Pyrexia			
subjects affected / exposed	10 / 49 (20.41%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	11	1	0
Sensation of foreign body			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 49 (12.24%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	6	1	0
Dry throat			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	6 / 49 (12.24%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	9	0	0
Epistaxis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hiccups			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			

subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	2 / 49 (4.08%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	2	2	0
Confusional state			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	4 / 49 (8.16%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	4	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 49 (8.16%)	3 / 30 (10.00%)	1 / 10 (10.00%)
occurrences (all)	8	4	1
Amylase increased			
subjects affected / exposed	4 / 49 (8.16%)	3 / 30 (10.00%)	1 / 10 (10.00%)
occurrences (all)	6	3	2
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 49 (10.20%)	3 / 30 (10.00%)	0 / 10 (0.00%)
occurrences (all)	9	3	0
Blood bilirubin increased			
subjects affected / exposed	3 / 49 (6.12%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Blood creatinine increased			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Blood iron decreased			

subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 49 (6.12%)	2 / 30 (6.67%)	2 / 10 (20.00%)
occurrences (all)	4	2	11
Lipase increased			
subjects affected / exposed	2 / 49 (4.08%)	2 / 30 (6.67%)	1 / 10 (10.00%)
occurrences (all)	2	4	7
Weight decreased			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	3 / 49 (6.12%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Limb injury			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Atrial fibrillation			

subjects affected / exposed	4 / 49 (8.16%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	7	1	1
Bradycardia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Sinus bradycardia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Dizziness			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Headache			
subjects affected / exposed	4 / 49 (8.16%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	4	1	1
Neuropathy peripheral			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Paraesthesia			
subjects affected / exposed	2 / 49 (4.08%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	2	2	0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	13 / 49 (26.53%)	4 / 30 (13.33%)	1 / 10 (10.00%)
occurrences (all)	15	5	2
Leukopenia			
subjects affected / exposed	4 / 49 (8.16%)	4 / 30 (13.33%)	1 / 10 (10.00%)
occurrences (all)	7	11	1
Lymphadenopathy			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Lymphopenia			
subjects affected / exposed	1 / 49 (2.04%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Neutropenia			
subjects affected / exposed	18 / 49 (36.73%)	7 / 30 (23.33%)	4 / 10 (40.00%)
occurrences (all)	36	13	11
Thrombocytopenia			
subjects affected / exposed	22 / 49 (44.90%)	12 / 30 (40.00%)	4 / 10 (40.00%)
occurrences (all)	56	21	14
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Swelling of eyelid			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	3 / 49 (6.12%)	3 / 30 (10.00%)	0 / 10 (0.00%)
occurrences (all)	4	5	0
Abdominal pain upper			
subjects affected / exposed	1 / 49 (2.04%)	3 / 30 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Constipation			
subjects affected / exposed	6 / 49 (12.24%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	6	2	0
Diarrhoea			
subjects affected / exposed	9 / 49 (18.37%)	7 / 30 (23.33%)	5 / 10 (50.00%)
occurrences (all)	16	8	10
Dry mouth			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	3 / 49 (6.12%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	4	2	0
Dysphagia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Faeces soft			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	5 / 49 (10.20%)	4 / 30 (13.33%)	0 / 10 (0.00%)
occurrences (all)	6	5	0
Odynophagia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Pancreatitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	5 / 49 (10.20%)	3 / 30 (10.00%)	1 / 10 (10.00%)
occurrences (all)	6	7	1
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cholecystocholangitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hepatocellular injury			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	7
Hyperbilirubinaemia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Blood blister			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Dermatitis bullous			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Dry skin			

subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Ecchymosis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	5 / 49 (10.20%)	5 / 30 (16.67%)	3 / 10 (30.00%)
occurrences (all)	11	5	7
Lividity			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Macule			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Onychoclasis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 49 (0.00%)	3 / 30 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Photosensitivity reaction			
subjects affected / exposed	2 / 49 (4.08%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	3	2	3
Pruritus			
subjects affected / exposed	4 / 49 (8.16%)	1 / 30 (3.33%)	3 / 10 (30.00%)
occurrences (all)	7	1	6
Purpura			
subjects affected / exposed	2 / 49 (4.08%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Rash			

subjects affected / exposed	6 / 49 (12.24%)	4 / 30 (13.33%)	2 / 10 (20.00%)
occurrences (all)	9	4	3
Rash macular			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	4
Rash maculo-papular			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Rash vesicular			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Skin hyperpigmentation			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 49 (4.08%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	2	4	0
Back pain			
subjects affected / exposed	6 / 49 (12.24%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	8	0	0
Muscle spasms			
subjects affected / exposed	6 / 49 (12.24%)	2 / 30 (6.67%)	2 / 10 (20.00%)
occurrences (all)	6	3	3
Myalgia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Clostridium difficile colitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Corona virus infection			
subjects affected / exposed	3 / 49 (6.12%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	8	1	4
Erysipelas			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Furuncle			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Genital infection fungal			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0

Oral fungal infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 30 (3.33%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Pneumonia			
subjects affected / exposed	0 / 49 (0.00%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Sinusitis			
subjects affected / exposed	1 / 49 (2.04%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 49 (2.04%)	3 / 30 (10.00%)	2 / 10 (20.00%)
occurrences (all)	3	3	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 49 (8.16%)	0 / 30 (0.00%)	2 / 10 (20.00%)
occurrences (all)	5	0	2
Hypercalcaemia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 30 (3.33%)	3 / 10 (30.00%)
occurrences (all)	1	1	3
Hyperkalaemia			

subjects affected / exposed	0 / 49 (0.00%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 49 (0.00%)	3 / 30 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Hyperuricaemia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 30 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 49 (2.04%)	2 / 30 (6.67%)	1 / 10 (10.00%)
occurrences (all)	1	4	1
Hypocalcaemia			
subjects affected / exposed	5 / 49 (10.20%)	4 / 30 (13.33%)	0 / 10 (0.00%)
occurrences (all)	8	6	0
Hypokalaemia			
subjects affected / exposed	6 / 49 (12.24%)	3 / 30 (10.00%)	1 / 10 (10.00%)
occurrences (all)	7	3	2
Hypomagnesaemia			
subjects affected / exposed	6 / 49 (12.24%)	2 / 30 (6.67%)	0 / 10 (0.00%)
occurrences (all)	10	2	0
Hyponatraemia			
subjects affected / exposed	3 / 49 (6.12%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Hypophosphataemia			
subjects affected / exposed	7 / 49 (14.29%)	6 / 30 (20.00%)	0 / 10 (0.00%)
occurrences (all)	8	12	0
Musculoskeletal pain			
subjects affected / exposed	4 / 49 (8.16%)	1 / 30 (3.33%)	0 / 10 (0.00%)
occurrences (all)	4	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2019	• Schedule of Events revised to for all participants to determine whether they met Exclusion Criterion 10. • Exclusion Criteria was modified to remove the notation from Exclusion Criterion 10. Criterion 15 was modified to add the exclusion of participants with tuberculosis infection. • Packaging and Storage was updated to match the ibrutinib Investigator's Brochure (IB). • Preparation and Administration was updated to include precautions concerning extravasation of loncastuximab tesirine based on updated safety information. • Loncastuximab Tesirine dosing was revised to clarify the criteria for using sequential dosing. • Dose Escalation Design was revised to specify a minimum of 5 days between dosing the first and second patient at each dose level during dose escalation (Part 1), and was also revised to allow enrollment of additional participants during the dose escalation phase at the discretion of the Dose Escalation Steering Committee (DESC). • Dose-Limiting Toxicity Definition was modified to clarify the non-hematologic DLT definition. • Loncastuximab Tesirine was revised to clarify criteria for dose hold and resumption for non-hematologic and hematologic toxicity. • Premedication for Loncastuximab Tesirine and Treatment and Prophylaxis of Infusion-Related to Hypersensitivity Reactions were modified to allow the use of intravenous (IV) dexamethasone. • Adverse Events of Special Interest (AESIs) was added to provide information regarding reporting the AESI of major hemorrhage. • Laboratory Tests added hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) testing. • Table 9 was revised to show updated PK time points for C5 and C6 • Adverse Events was revised to clarify which treatment-emergent adverse events (TEAEs) were included in the statistical analysis.
09 January 2020	• Based on the observed complete response (CR) rate in participants who were enrolled and treated with loncastuximab tesirine and ibrutinib in Part 1, this trial was amended to a Phase 1/2 protocol. • The trial expanded enrollment to allow GCB DLBCL patients on study treatment. • The trial sample size was increased to approximately 161 patients, and Phase 2 evaluated efficacy in non-GCB DLBCL participants as its primary endpoint. • Supplementary secondary endpoints were added.
14 May 2020	• The trial was amended to allow for additional doses of loncastuximab tesirine to be administered on Day 1 of Cycles 5, 6, 9 and 10 in the Phase 2 portion of the study. • In addition, the Sponsor on a case-by-case review could have allowed participants benefitting clinically at 1 year to receive additional doses of study drug(s).

26 March 2021	• Extended the contraception duration for applicable participants to align with the current regulatory guidance; to update guidance to investigators regarding loncastuximab tesirine dose delays and modifications as well as prohibited medication for concurrent use with loncastuximab tesirine; and removed the loncastuximab tesirine dose adjustment for participants with a body mass index (BMI) ≥35kg/m^2. • Provided two clarifications: one regarding patient reported outcome (PRO) collection time points during the study follow-up and the other notifying that mantle cell lymphoma (MCL) participants enrolled into the Phase 2 part of the study will have central reviews of their scans. • Incorporated all country specific amendments from the country specific protocols to a global protocol to eliminate country specific protocols going forward.
31 August 2021	• Amended the study design for the Phase 2 by enrolling approximately 100 participants with relapsed or refractory Diffuse Large B-Cell Lymphoma (DLBCL) to a new treatment cohort in which loncastuximab tesirine will be given every cycle (rather than intermittently) in combination with ibrutinib.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 November 2022	The study was early terminated before enrolling participants into the new, planned treatment cohort.	-

Notes:

Limitations and caveats

None reported