



Clinical trial results:

An Open-Label, Multicenter, Phase 1/2 Study of Tazemetostat (EZH2 Histone Methyl Transferase [HMT] Inhibitor) as a Single Agent in Subjects With Advanced Solid Tumors or With B-Cell Lymphomas and Tazemetostat in Combination with Prednisolone in Subjects with Diffuse Large B Cell Lymphoma

Summary

EudraCT number	2012-004083-21
Trial protocol	GB DE
Global end of trial date	02 November 2021

Results information

Result version number	v2 (current)
This version publication date	23 December 2023
First version publication date	18 November 2022
Version creation reason	• Correction of full data set • Need to update the study results

Trial information

Trial identification

Sponsor protocol code	E7438-G000-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01897571
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Epizyme, Inc.
Sponsor organisation address	400 Technology Square, Cambridge, Massachusetts, United States, 02139
Public contact	Medical Lead or Designee, Epizyme, Inc., +1 855500-1011, clinicaltrials@epizyme.com
Scientific contact	Medical Lead or Designee, Epizyme, Inc., +1 855500-1011, clinicaltrials@epizyme.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	02 November 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1: To determine the recommended Phase 2 dose (RP2D) of tazemetostat as a single agent administered orally twice daily (BID), continuously in 28-day cycles, in patients with advanced solid tumors or relapsed and/or refractory (R/R) B-cell lymphomas.

Phase 2: To determine the objective response rate [ORR; complete response (CR) + partial response (PR)] of tazemetostat in patients with enhancer of zeste homolog 2 (EZH2) gene mutation positive (MT) or negative [wild-type (WT)] with histologically confirmed diffuse large B-cell lymphoma (DLBCL) or follicular lymphomas (FL) with R/R disease and the ORR of tazemetostat in combination with prednisolone in patients with EZH2 WT DLBCL.

Protection of trial subjects:

The procedures set out in the study protocol pertaining to the conduct, evaluation, and documentation of this study were designed to ensure that the Sponsor and Investigators abide by Good Clinical Practice as described in the International Conference on Harmonisation Tripartite Guideline E6 (R1), and for United States Investigators, 21 Code of Federal Regulations Parts 50, 54, 56, and 312. Compliance with these regulations also constituted compliance with the ethical principles described in the current revision of the Declaration of Helsinki. The study was also carried out in keeping with local legal and regulatory requirements.

Background therapy:

Phase 2: The DLBCL patients with EZH2 WT received prednisolone 40 milligram per square meter (mg/m²) on Days 1 to 5 and 15 to 19 from Cycle 1 to 4 as background therapy.

Evidence for comparator: -

Actual start date of recruitment	13 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 255
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	United States: 34
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	United Kingdom: 58

Worldwide total number of subjects	400
EEA total number of subjects	274

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)	196
From 65 to 84 years	198
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

This Phase 1/2, open-label study was conducted in patients with advanced solid tumors or with B-cell lymphomas or DLBCL at 39 clinical sites. A total of 401 patients were enrolled in the study. Of which, 400 patients were treated.

Pre-assignment

Screening details:

Phase 1 and Phase 2 part of the study consisted of a screening period (up to 28 days) followed by continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. Patients who remained on tazemetostat for 24 months or longer and who were eligible were transferred to a rollover study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: Tazemetostat 100 mg

Arm description:

Patients received tazemetostat 100 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 100 mg BID administered orally with or without food in continuous 28-day treatment cycles.

Arm title	Phase 1: Tazemetostat 200 mg
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Arm description:

Patients received tazemetostat 200 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 200 mg BID administered orally with or without food in continuous 28-day treatment cycles.

Arm title	Phase 1: Tazemetostat 400 mg
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Arm description:

Patients received tazemetostat 400 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
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Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 400 mg BID administered orally with or without food in continuous 28-day treatment cycles.

Arm title	Phase 1: Tazemetostat 800 mg
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Arm description:

Patients received tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 800 mg BID administered orally with or without food in continuous 28-day treatment cycles.

Arm title	Phase 1: Tazemetostat 1600 mg
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Arm description:

Patients received tazemetostat 1600 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 1600 mg BID administered orally with or without food in continuous 28-day treatment cycles.

Arm title	Phase 1: Food Effect (All Patients)
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Arm description:

Patients received tazemetostat 200 mg as a single oral dose on Day -8 either after fasting for 8 hours before dosing or immediately after consuming a high-fat breakfast on Day -8. Following a 7-day washout period, patients crossed over to receive the second tazemetostat 200 mg single oral dose on Day -1 in the opposite condition (fed or fasted).

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 200 mg administered orally with or without food as per fasted and fed conditions.

Arm title	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg
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Arm description:

Patients received tazemetostat 800 mg orally BID continuously starting on Day 1, with a single oral dose of midazolam 2 mg administered on Day -1 and then on Day 15. Post Day 15, patients continued to receive tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed

disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 800 mg BID administered orally BID in continuous 28-day treatment cycles.

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

Dosage and administration details:

Midazolam 2 mg single dose was administered orally on Day -1 and 15.

Arm title	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2
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Arm description:

Patients with R/R FL with mutant EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 800 mg twice daily administered orally as 4*200 mg tablets with or without food in continuous 28-day treatment cycles.

Arm title	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
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Arm description:

Patients with R/R FL with wild-type EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tazemetostat 800 mg twice daily administered orally as 4*200 mg tablets with or without food in continuous 28-day treatment cycles.

Arm title	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy
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Arm description:

Patients with R/R DLBCL received 800 mg of tazemetostat monotherapy, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
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Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Tazemetostat 800 mg twice daily administered orally as 4*200 mg tablets with or without food in continuous 28-day treatment cycles	
Arm title	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy

Arm description:

Patients received tazemetostat (taze) 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. In addition, these patients also received prednisolone 40 mg/m² on Days 1 to 5 and 15 to 19 from Cycle 1 to Cycle 4 post which tazemetostat monotherapy was continued.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438, E7438
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Tazemetostat 800 mg twice daily administered orally as 4*200 mg tablets with or without food in continuous 28-day treatment cycles.	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisolone 40 mg/m² once daily was administered on Days 1 to 5 and 15 to 19 from Cycle 1 to Cycle 4.

Number of subjects in period 1	Phase 1: Tazemetostat 100 mg	Phase 1: Tazemetostat 200 mg	Phase 1: Tazemetostat 400 mg
Started	6	3	3
Completed	0	1	0
Not completed	6	2	3
Enrolled in rollover study	-	-	-
Consent withdrawn by subject	-	-	-
Death	2	2	3
Unspecified	1	-	-
Lost to follow-up	3	-	-

Number of subjects in period 1	Phase 1: Tazemetostat 800 mg	Phase 1: Tazemetostat 1600 mg	Phase 1: Food Effect (All Patients)
Started	14	12	13

Completed	5	0	0
Not completed	9	12	13
Enrolled in rollover study	-	-	-
Consent withdrawn by subject	-	-	-
Death	6	7	9
Unspecified	3	3	4
Lost to follow-up	-	2	-

Number of subjects in period 1	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
Started	13	48	54
Completed	1	16	19
Not completed	12	32	35
Enrolled in rollover study	-	9	7
Consent withdrawn by subject	-	1	4
Death	5	22	23
Unspecified	7	-	-
Lost to follow-up	-	-	1

Number of subjects in period 1	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Started	163	71
Completed	20	6
Not completed	143	65
Enrolled in rollover study	9	1
Consent withdrawn by subject	3	1
Death	129	59
Unspecified	-	-
Lost to follow-up	2	4

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: Tazemetostat 100 mg
Reporting group description: Patients received tazemetostat 100 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 200 mg
Reporting group description: Patients received tazemetostat 200 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 400 mg
Reporting group description: Patients received tazemetostat 400 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 800 mg
Reporting group description: Patients received tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 1600 mg
Reporting group description: Patients received tazemetostat 1600 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Food Effect (All Patients)
Reporting group description: Patients received tazemetostat 200 mg as a single oral dose on Day -8 either after fasting for 8 hours before dosing or immediately after consuming a high-fat breakfast on Day -8. Following a 7-day washout period, patients crossed over to receive the second tazemetostat 200 mg single oral dose on Day -1 in the opposite condition (fed or fasted).	
Reporting group title	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg
Reporting group description: Patients received tazemetostat 800 mg orally BID continuously starting on Day 1, with a single oral dose of midazolam 2 mg administered on Day -1 and then on Day 15. Post Day 15, patients continued to receive tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2
Reporting group description: Patients with R/R FL with mutant EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
Reporting group description: Patients with R/R FL with wild-type EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy
Reporting group description: Patients with R/R DLBCL received 800 mg of tazemetostat monotherapy, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Reporting group description: Patients received tazemetostat (taze) 800 mg tablets orally BID in continuous 28-day treatment cycles	

until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. In addition, these patients also received prednisolone 40 mg/m² on Days 1 to 5 and 15 to 19 from Cycle 1 to Cycle 4 post which tazemetostat monotherapy was continued.

Reporting group values	Phase 1: Tazemetostat 100 mg	Phase 1: Tazemetostat 200 mg	Phase 1: Tazemetostat 400 mg
Number of subjects	6	3	3
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	51.5 ± 15.74	55.0 ± 30.20	59.0 ± 7.00
Gender categorical Units: Subjects			
Female	1	1	0
Male	5	2	3
Ethnicity			
Unknown or Not Reported category included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	1	2
Unknown or Not Reported	4	2	1
Race			
Unknown or Not Reported included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	1	2
More than one race	0	0	0
Unknown or Not Reported	4	2	1

Reporting group values	Phase 1: Tazemetostat 800 mg	Phase 1: Tazemetostat 1600 mg	Phase 1: Food Effect (All Patients)
Number of subjects	14	12	13
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	56.4 ± 13.54	51.6 ± 21.42	53.2 ± 16.39
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Gender categorical			
Units: Subjects			
Female	4	5	7
Male	10	7	6
Ethnicity			
Unknown or Not Reported category included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	6	10
Unknown or Not Reported	7	6	3
Race			
Unknown or Not Reported included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	6	10
More than one race	0	0	0
Unknown or Not Reported	7	6	3

Reporting group values	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
Number of subjects	13	48	54
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	55.0	62.0	61.1
standard deviation	± 13.66	± 8.83	± 11.38
Gender categorical			
Units: Subjects			
Female	8	26	20
Male	5	22	34
Ethnicity			
Unknown or Not Reported category included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
Hispanic or Latino	0	0	3
Not Hispanic or Latino	11	38	26
Unknown or Not Reported	2	10	25
Race			
Unknown or Not Reported included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	11	33	15
More than one race	0	0	0
Unknown or Not Reported	2	15	38

Reporting group values	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy	Total
Number of subjects	163	71	400
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	63.2 ± 14.35	65.4 ± 11.78	-
Gender categorical Units: Subjects			
Female	72	32	176
Male	91	39	224
Ethnicity			
Unknown or Not Reported category included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
Hispanic or Latino	3	1	7
Not Hispanic or Latino	103	62	268
Unknown or Not Reported	57	8	125
Race			
Unknown or Not Reported included patients for whom race and/or ethnicity were not obtained due to local privacy regulations.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	1	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	71	28	186
More than one race	0	0	0
Unknown or Not Reported	89	41	208

End points

End points reporting groups

Reporting group title	Phase 1: Tazemetostat 100 mg
Reporting group description: Patients received tazemetostat 100 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 200 mg
Reporting group description: Patients received tazemetostat 200 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 400 mg
Reporting group description: Patients received tazemetostat 400 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 800 mg
Reporting group description: Patients received tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Tazemetostat 1600 mg
Reporting group description: Patients received tazemetostat 1600 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 1: Food Effect (All Patients)
Reporting group description: Patients received tazemetostat 200 mg as a single oral dose on Day -8 either after fasting for 8 hours before dosing or immediately after consuming a high-fat breakfast on Day -8. Following a 7-day washout period, patients crossed over to receive the second tazemetostat 200 mg single oral dose on Day -1 in the opposite condition (fed or fasted).	
Reporting group title	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg
Reporting group description: Patients received tazemetostat 800 mg orally BID continuously starting on Day 1, with a single oral dose of midazolam 2 mg administered on Day -1 and then on Day 15. Post Day 15, patients continued to receive tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2
Reporting group description: Patients with R/R FL with mutant EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
Reporting group description: Patients with R/R FL with wild-type EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy
Reporting group description: Patients with R/R DLBCL received 800 mg of tazemetostat monotherapy, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Reporting group description: Patients received tazemetostat (taze) 800 mg tablets orally BID in continuous 28-day treatment cycles	

until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. In addition, these patients also received prednisolone 40 mg/m² on Days 1 to 5 and 15 to 19 from Cycle 1 to Cycle 4 post which tazemetostat monotherapy was continued.

Subject analysis set title	Phase I
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients in the Phase 1 portion of the study. Tazemetostat: Patients who received 100 mg to 1600 mg of tazemetostat, BID, administered in continuous 28-day cycles.

Primary: RP2D of Tazemetostat as a Single-Agent and in Combination With Prednisolone (Phase 1 Only)

End point title	RP2D of Tazemetostat as a Single-Agent and in Combination With Prednisolone (Phase 1 Only) ^[1]
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End point description:

The RP2D of tazemetostat as administered orally BID, continuously in 28-day cycles in patients with advanced solid tumors or with R/R B-cell lymphomas as determined by incidence, seriousness, toxicity grade, and relatedness of treatment emergent dose limiting toxicities (DLTs).

End point type	Primary
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End point timeframe:

The first 28-day cycle of therapy

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Phase I			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: mg BID				
number (not applicable)	800			

Statistical analyses

No statistical analyses for this end point

Primary: ORR (CR + PR) (Phase 2)

End point title	ORR (CR + PR) (Phase 2) ^{[2][3]}
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End point description:

Number of patients achieving an objective response (CR or PR)/number of patients treated x 100%. ORR was calculated as the percentage of patients with a confirmed CR or PR relative to the total number of patients in the analysis population per response evaluation criteria in solid tumors (RECIST) version (v)1.1. CR was defined as disappearance of all target and non-target lesions and any pathological lymph nodes must be <10 millimeter (mm) in the short axis. PR was defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference, the baseline sum of the diameters.

End point type	Primary
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End point timeframe:

Radiologic tumor assessments performed at baseline(within 28 days before start of study treatment)and every 8 weeks during Cycles 2 to 6,and then every 12 weeks thereafter until confirmed disease progression (PD)/death,a maximum of approximately 82 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was performed for the primary endpoint.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only patients treated in Phase 2 part of the study were analyzed in this endpoint.

End point values	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	54	163	71
Units: Count of participants				
number (not applicable)	34	19	30	8

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) for Tazemetostat as a Single Agent or in Combination With Prednisolone (Phase 2 Only)

End point title	Duration of Response (DOR) for Tazemetostat as a Single Agent or in Combination With Prednisolone (Phase 2 Only) ^[4]
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End point description:

The time (in months) from the date of the initial response (CR or PR, whichever was first) until the date of the first documented disease progression per an Independent Review Committee or per Investigator or death due to any cause. Patients who were alive and progression free at the time of the analysis were censored at the last date where the patient was known to be in response. Per RECIST v.1.0, CR was defined as disappearance of all target and non-target lesions and any pathological lymph nodes must be <10 mm in the short axis. The PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as a reference, the baseline sum of diameters. Patients who had a CR or PR per an Independent Review Committee were included in this analysis. 99999 = Upper limit of confidence interval (CI) was not estimable due to insufficient number of participants with events at study closure.

End point type	Secondary
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End point timeframe:

Radiologic tumor assessments performed at baseline (within 28 days before start of study treatment) and every 8 weeks during Cycles 2 to 6, and then every 12 weeks thereafter until confirmed PD/death, a maximum of approximately 82 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only patients treated in Phase 2 part of the study were analyzed in this endpoint.

End point values	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	19	163	71
Units: months				

median (confidence interval 95%)	11.3 (7.2 to 99999)	13.0 (5.6 to 99999)	5.8 (3.7 to 12.8)	5.7 (2.1 to 99999)
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Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) for Tazemetostat as a Single Agent or in Combination With Prednisolone (Phase 2 Only)

End point title	Progression Free Survival (PFS) for Tazemetostat as a Single Agent or in Combination With Prednisolone (Phase 2 Only) ^[5]
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End point description:

The time (in months) from the date of first dose of tazemetostat until the earliest date of disease progression or death from any cause. Per RECIST v1.0, CR was defined as disappearance of all target and non-target lesions and any pathological lymph nodes must be <10 mm in the short axis. The PR was defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference, the baseline sum of the diameters. Patients who had a response event per Independent Review Committee were included in this analysis.

End point type	Secondary
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End point timeframe:

Radiologic tumor assessments performed at baseline (within 28 days before start of study treatment) and every 8 weeks during Cycles 2 to 6, and then every 12 weeks thereafter until confirmed PD/death, a maximum of approximately 82 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only patients treated in Phase 2 part of the study were analyzed in this endpoint.

End point values	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	54	163	71
Units: months				
median (confidence interval 95%)	13.8 (10.9 to 22.1)	11.1 (3.7 to 14.6)	1.9 (1.8 to 3.2)	1.8 (1.6 to 2.0)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are reported from the first dose of study drug (Day 1) until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. A maximum of approximately 40 months for Phase 1 and 82 months for Phase 2

Adverse event reporting additional description:

The safety population included all patients in the Intent-to-treat (ITT) population set who had at least 1 post-dose safety observation recorded. MedDRA v17.1 for Phase 1 and MedDRA v18.1 for Phase 2.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.03
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Reporting groups

Reporting group title	Phase 1: Tazemetostat 100 mg
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Reporting group description:

Patients received tazemetostat 100 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 1: Tazemetostat 200 mg
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Reporting group description:

Patients received tazemetostat 200 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 1: Tazemetostat 400 mg
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Reporting group description:

Patients received tazemetostat 400 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 1: Tazemetostat 800 mg
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Reporting group description:

Patients received tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 1: Tazemetostat 1600 mg
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Reporting group description:

Patients received tazemetostat 1600 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 1: Food Effect (All Patients)
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Reporting group description:

Patients received tazemetostat 200 mg as a single oral dose on Day -8 either after fasting for 8 hours before dosing or immediately after consuming a high-fat breakfast on Day -8. Following a 7-day washout period, patients crossed over to receive the second tazemetostat 200 mg single oral dose on Day -1 in the opposite condition (fed or fasted).

Reporting group title	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg
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Reporting group description:

Patients received tazemetostat 800 mg orally BID continuously starting on Day 1, with a single oral dose of midazolam 2 mg administered on Day -1 and then on Day 15. Post Day 15, patients continued to receive tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2
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Reporting group description:

Patients with R/R FL with mutant EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
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Reporting group description:

Patients with R/R FL with wild-type EZH2 treated with tazemetostat as a single agent in Phase 2 of the study. Patients received 800 mg of tazemetostat, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy
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Reporting group description:

Patients with R/R DLBCL received 800 mg of tazemetostat monotherapy, orally BID, administered in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy
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Reporting group description:

Patients received tazemetostat 800 mg tablets orally BID in continuous 28-day treatment cycles until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. In addition, these patients also received prednisolone 40 mg/m² on Days 1 to 5 and 15 to 19 from Cycle 1 to Cycle 4 post which tazemetostat monotherapy was continued.

Serious adverse events	Phase 1: Tazemetostat 100 mg	Phase 1: Tazemetostat 200 mg	Phase 1: Tazemetostat 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Acute myeloid leukaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 transformation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Malignant melanoma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Femoral artery occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
General physical health deterioration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Generalised oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Axillary pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Breakthrough pain				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Chills				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Fatigue				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Malaise				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Non-cardiac chest pain				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Pain				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Multi-organ failure				

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Prostatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Acute pulmonary oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Mediastinal disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Tonsillar hypertrophy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 uric acid increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Creatinine renal clearance abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 condition abnormal			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Liver function test abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Femoral neck fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hip fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Toxicity to various agents			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Diastolic dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 constrictive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Osmotic demyelination syndrome			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Post herpetic neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Transient global amnesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lethargy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Spinal cord compression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
8th nerve paralysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Histiocytosis haematophagic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pancreatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Duodenal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastric disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastric ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastric ulcer perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Melaena			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pancreatitis acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Subileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Jaundice			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Portal hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Renal colic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Anuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Device related infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Empyema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Septic shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Bronchopneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Encephalitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Febrile infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Dehydration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyperamylasaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lactic acidosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 1: Tazemetostat 800 mg	Phase 1: Tazemetostat 1600 mg	Phase 1: Food Effect (All Patients)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	5 / 12 (41.67%)	6 / 13 (46.15%)
number of deaths (all causes)	0	2	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 transformation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Malignant melanoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Cancer pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Orthostatic hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral artery occlusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Superior vena cava syndrome			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Axillary pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Breakthrough pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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

Chills			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Multi-organ failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Prostatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 distress			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (7.14%)	0 / 12 (0.00%)	0 / 13 (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
Hypoxia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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

Acute pulmonary oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 exertional			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Mediastinal disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Pneumonitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			

Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 13 (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
Depression			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (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
Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Amylase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 creatinine increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 uric acid increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Creatinine renal clearance abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 condition abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Liver function test abnormal			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Femoral neck fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hip fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Toxicity to various agents			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Diastolic dysfunction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 constrictive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Neuralgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osmodic demyelination syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Post herpetic neuralgia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Transient global amnesia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Encephalopathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Headache			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Lethargy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 disorder			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Sciatica			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Spinal cord compression			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
8th nerve paralysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (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
Neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 13 (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
Histiocytosis haematophagic			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Lymphopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Duodenal obstruction			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Gastric disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Gastric ulcer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Gastric ulcer perforation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Intestinal obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Melaena			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Pancreatitis acute			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Subileus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Jaundice			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Jaundice cholestatic			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Portal hypertension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Renal colic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Anuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			

Hypercalcaemia of malignancy subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (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
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Bone pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Pain in jaw			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Empyema				
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (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	
Lung infection				
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 13 (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	
Septic shock				
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 13 (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	
Herpes zoster				
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 pneumonia				
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	
Bronchitis				
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	
Bronchopneumonia				
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Clostridium difficile colitis				
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	
Encephalitis				

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Febrile infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Oral candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Rhinovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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			
Decreased appetite			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hyperamylasaemia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hypercalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hyperuricaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hypokalaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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
Lactic acidosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 13 (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 1: Tazemetostat 800 mg + Midazolam 2	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant	Phase 2 Group 2: Tazemetostat in R/R FL With Wild-Type
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	mg	EZH2	EZH2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)	14 / 48 (29.17%)	16 / 54 (29.63%)
number of deaths (all causes)	0	2	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Acute myeloid leukaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lymphoma transformation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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

Myelodysplastic syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Orthostatic hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Femoral artery occlusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
General physical health deterioration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Axillary pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Breakthrough pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Chills			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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

Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Multi-organ failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Prostatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 distress			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Acute pulmonary oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 exertional			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Mediastinal disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pneumonitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Depression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Confusional state			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Amylase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 creatinine increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 uric acid increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Creatinine renal clearance abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 condition abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Liver function test abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			

Femoral neck fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hip fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Toxicity to various agents			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Diastolic dysfunction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 constrictive			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Cervicobrachial syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 48 (0.00%)	0 / 54 (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
Neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Osmotic demyelination syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Post herpetic neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Transient global amnesia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Sciatica			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Spinal cord compression			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
8th nerve paralysis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histiocytosis haematophagic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	1 / 48 (2.08%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Duodenal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Gastric disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Gastric ulcer perforation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Melaena			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pancreatitis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
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 haemorrhage			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Subileus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Portal hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			

Renal colic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Haematuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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

Back pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Bone pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Pain in jaw			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Empyema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Lung infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 48 (2.08%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Bronchopneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Encephalitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Febrile infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Influenza			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Rhinovirus infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 infection			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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			
Decreased appetite			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hyperamylasaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hyperglycaemia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hyperuricaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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
Lactic acidosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 48 (0.00%)	0 / 54 (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 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 163 (51.53%)	47 / 71 (66.20%)	
number of deaths (all causes)	34	18	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			

subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma transformation			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	2 / 163 (1.23%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			

subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery occlusion			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	9 / 163 (5.52%)	8 / 71 (11.27%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthenia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 163 (0.61%)	3 / 71 (4.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Axillary pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breakthrough pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			

subjects affected / exposed	0 / 163 (0.00%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	2 / 163 (1.23%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Multi-organ failure			
subjects affected / exposed	0 / 163 (0.00%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory distress			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 163 (0.61%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 163 (0.00%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			

subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinal disorder			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Amylase increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood uric acid increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance abnormal			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	2 / 163 (1.23%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hip fracture			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis constrictive			

subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osmotic demyelination syndrome			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
8th nerve paralysis			

subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 163 (1.84%)	3 / 71 (4.23%)	
occurrences causally related to treatment / all	2 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	8 / 163 (4.91%)	7 / 71 (9.86%)	
occurrences causally related to treatment / all	5 / 10	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 163 (0.61%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	12 / 163 (7.36%)	7 / 71 (9.86%)	
occurrences causally related to treatment / all	12 / 14	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	5 / 163 (3.07%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	2 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric disorder			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			

subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Large intestinal obstruction			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			

subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 163 (1.84%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in jaw			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 163 (0.61%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	2 / 163 (1.23%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			

subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 163 (0.00%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	0 / 163 (0.00%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 163 (0.61%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperamylasaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			

subjects affected / exposed	1 / 163 (0.61%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase 1: Tazemetostat 100 mg	Phase 1: Tazemetostat 200 mg	Phase 1: Tazemetostat 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	5	1	1
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1
Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

Non-serious adverse events	Phase 1: Tazemetostat 800 mg	Phase 1: Tazemetostat 1600 mg	Phase 1: Food Effect (All Patients)
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 14 (85.71%)	11 / 12 (91.67%)	12 / 13 (92.31%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 3	0 / 12 (0.00%) 0	0 / 13 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	4 / 12 (33.33%) 4	0 / 13 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	1 / 12 (8.33%) 2	2 / 13 (15.38%) 4
Thrombocytopenia			

subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 14	1 / 12 (8.33%) 3	4 / 13 (30.77%) 6
Neutropenia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 3	2 / 12 (16.67%) 2	1 / 13 (7.69%) 1
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	10 / 14 (71.43%) 4	4 / 12 (33.33%) 5	7 / 13 (53.85%) 9
Pyrexia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2	3 / 12 (25.00%) 3	0 / 13 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	2 / 13 (15.38%) 2
Fatigue subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2	0 / 12 (0.00%) 0	0 / 13 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	6 / 12 (50.00%) 7	3 / 13 (23.08%) 5
Vomiting subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3	1 / 12 (8.33%) 2	2 / 13 (15.38%) 2
Constipation subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3	2 / 12 (16.67%) 2	3 / 13 (23.08%) 3
Abdominal pain subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 4	0 / 12 (0.00%) 0	2 / 13 (15.38%) 3
Diarrhoea subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3	2 / 12 (16.67%) 2	0 / 13 (0.00%) 0
Abdominal pain upper			

subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	2 / 12 (16.67%)	2 / 13 (15.38%)
occurrences (all)	1	2	2
Cough			
subjects affected / exposed	2 / 14 (14.29%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	4	3	1
Dyspnoea exertional			
subjects affected / exposed	2 / 14 (14.29%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	2	3	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 14 (14.29%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences (all)	2	1	2
Night sweats			
subjects affected / exposed	3 / 14 (21.43%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	3	1	0
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	6 / 14 (42.86%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	6	2	1
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Infections and infestations			
Urinary tract infection			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 12 (8.33%) 1	1 / 13 (7.69%) 1
Bronchitis subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3	0 / 12 (0.00%) 0	0 / 13 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 12 (0.00%) 0	0 / 13 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	0 / 13 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3	2 / 12 (16.67%) 3	3 / 13 (23.08%) 4
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	0 / 12 (0.00%) 0	2 / 13 (15.38%) 2

Non-serious adverse events	Phase 1: Tazemetostat 800 mg + Midazolam 2 mg	Phase 2 Group 1: Tazemetostat in R/R FL With Mutant EZH2	Phase 2 Group 2: Tazemetostat in R/ R FL With Wild-Type EZH2
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 13 (100.00%)	46 / 48 (95.83%)	53 / 54 (98.15%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	6 / 48 (12.50%) 7	8 / 54 (14.81%) 8
Dysgeusia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 3	6 / 48 (12.50%) 6	2 / 54 (3.70%) 3
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	6 / 13 (46.15%) 8	3 / 48 (6.25%) 11	10 / 54 (18.52%) 16
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 48 (8.33%) 13	5 / 54 (9.26%) 10

Neutropenia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	4 / 48 (8.33%) 6	4 / 54 (7.41%) 6
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	7 / 13 (53.85%) 13	7 / 48 (14.58%) 9	12 / 54 (22.22%) 19
Pyrexia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 48 (4.17%) 2	8 / 54 (14.81%) 12
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	5 / 48 (10.42%) 6	3 / 54 (5.56%) 5
Fatigue subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	9 / 48 (18.75%) 14	9 / 54 (16.67%) 11
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	10 / 48 (20.83%) 15	14 / 54 (25.93%) 18
Vomiting subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	5 / 48 (10.42%) 9	7 / 54 (12.96%) 11
Constipation subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	5 / 48 (10.42%) 5	3 / 54 (5.56%) 4
Abdominal pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	8 / 48 (16.67%) 11	5 / 54 (9.26%) 6
Diarrhoea subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	11 / 48 (22.92%) 15	10 / 54 (18.52%) 18
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	5 / 48 (10.42%) 8	2 / 54 (3.70%) 2
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	3 / 48 (6.25%) 5	6 / 54 (11.11%) 9
Cough subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 3	7 / 48 (14.58%) 13	11 / 54 (20.37%) 15
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 48 (2.08%) 1	0 / 54 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	3 / 48 (6.25%) 3	1 / 54 (1.85%) 1
Night sweats subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 48 (6.25%) 3	1 / 54 (1.85%) 1
Alopecia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	11 / 48 (22.92%) 13	7 / 54 (12.96%) 7
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 48 (8.33%) 5	3 / 54 (5.56%) 4
Musculoskeletal and connective tissue disorders			
Muscle spasms subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 4	4 / 48 (8.33%) 7	6 / 54 (11.11%) 10
Back pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	7 / 48 (14.58%) 9	6 / 54 (11.11%) 9
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	5 / 48 (10.42%) 8	2 / 54 (3.70%) 4
Bronchitis			

subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	6 / 48 (12.50%) 11	9 / 54 (16.67%) 20
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 48 (8.33%) 4	5 / 54 (9.26%) 5
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	13 / 48 (27.08%) 16	7 / 54 (12.96%) 18
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	6 / 48 (12.50%) 6	2 / 54 (3.70%) 3
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 48 (4.17%) 2	1 / 54 (1.85%) 2

Non-serious adverse events	Phase 2 Group 3: Tazemetostat in R/R DLBCL Monotherapy	Phase 2 G4 :Taze+Prednisolone in R/R DLBCL Combination Therapy	
Total subjects affected by non-serious adverse events subjects affected / exposed	147 / 163 (90.18%)	56 / 71 (78.87%)	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	7 / 163 (4.29%) 7	2 / 71 (2.82%) 3	
Dysgeusia subjects affected / exposed occurrences (all)	7 / 163 (4.29%) 7	2 / 71 (2.82%) 2	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	25 / 163 (15.34%) 44	13 / 71 (18.31%) 30	
Thrombocytopenia subjects affected / exposed occurrences (all)	37 / 163 (22.70%) 83	13 / 71 (18.31%) 29	
Neutropenia			

subjects affected / exposed occurrences (all)	16 / 163 (9.82%) 32	7 / 71 (9.86%) 12	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	16 / 163 (9.82%)	15 / 71 (21.13%)	
occurrences (all)	25	16	
Pyrexia			
subjects affected / exposed	25 / 163 (15.34%)	7 / 71 (9.86%)	
occurrences (all)	35	8	
Oedema peripheral			
subjects affected / exposed	12 / 163 (7.36%)	8 / 71 (11.27%)	
occurrences (all)	14	8	
Fatigue			
subjects affected / exposed	23 / 163 (14.11%)	7 / 71 (9.86%)	
occurrences (all)	27	8	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	36 / 163 (22.09%)	9 / 71 (12.68%)	
occurrences (all)	40	12	
Vomiting			
subjects affected / exposed	23 / 163 (14.11%)	12 / 71 (16.90%)	
occurrences (all)	32	17	
Constipation			
subjects affected / exposed	14 / 163 (8.59%)	4 / 71 (5.63%)	
occurrences (all)	14	4	
Abdominal pain			
subjects affected / exposed	12 / 163 (7.36%)	12 / 71 (16.90%)	
occurrences (all)	14	21	
Diarrhoea			
subjects affected / exposed	28 / 163 (17.18%)	11 / 71 (15.49%)	
occurrences (all)	38	16	
Abdominal pain upper			
subjects affected / exposed	8 / 163 (4.91%)	2 / 71 (2.82%)	
occurrences (all)	10	2	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	7 / 163 (4.29%) 11	2 / 71 (2.82%) 2	
Cough subjects affected / exposed occurrences (all)	32 / 163 (19.63%) 37	6 / 71 (8.45%) 9	
Dyspnoea exertional subjects affected / exposed occurrences (all)	2 / 163 (1.23%) 2	0 / 71 (0.00%) 0	
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	3 / 163 (1.84%) 3	0 / 71 (0.00%) 0	
Night sweats subjects affected / exposed occurrences (all)	3 / 163 (1.84%) 5	2 / 71 (2.82%) 2	
Alopecia subjects affected / exposed occurrences (all)	6 / 163 (3.68%) 8	2 / 71 (2.82%) 3	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 163 (1.23%) 2	3 / 71 (4.23%) 3	
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	7 / 163 (4.29%) 9	2 / 71 (2.82%) 2	
Back pain subjects affected / exposed occurrences (all)	16 / 163 (9.82%) 22	4 / 71 (5.63%) 5	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	12 / 163 (7.36%) 17	3 / 71 (4.23%) 3	
Bronchitis			

subjects affected / exposed occurrences (all)	10 / 163 (6.13%) 13	5 / 71 (7.04%) 8	
Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 163 (3.68%) 6	2 / 71 (2.82%) 2	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 163 (4.91%) 15	1 / 71 (1.41%) 2	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	13 / 163 (7.98%) 16	10 / 71 (14.08%) 11	
Hypophosphataemia subjects affected / exposed occurrences (all)	3 / 163 (1.84%) 3	3 / 71 (4.23%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2013	Text was added to clarify that the follow-up schedule for survival was to occur every 12 weeks and to warn of the possibility of phototoxicity during prolonged exposure to sunlight. Additional clarification was added concerning safety data review for the purposes of dose escalation or maximum tolerated dose confirmation, contraception requirements were updated, and an exclusion criterion was added for patients with fructose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase deficiency.
24 April 2013	An updated description of the container holding the powder used for the oral suspension formulation was added.
19 June 2013	Information about the independent data monitoring committee and tazemetostat tablet formulation used in the study was added. Further, references to "serum" were changed to "plasma" in the text describing biomarker and pharmacogenetic assessments, and clarifying text was added to detail the exposure and pharmacokinetic (PK) parameters for both the tablet and oral suspension formulations. Additional detail was inserted to describe the formulation, strength, and container for the tazemetostat tablets and the required preparation procedures for the powder used in the oral suspension formulation.
22 October 2013	Text was added to clarify that the food effect (FE) and drug-drug interaction (DDI) parts of the study would be performed in parallel; to state that no newly enrolled patients were to receive powder for the oral suspension formulation and that instead, all patients were to receive the tablet formulation; to remove the restriction on the maximum daily tablet dose of 1000 mg; and to update the specified tazemetostat preparation procedures.
24 February 2014	A change was made to allow 6 patients to be enrolled in a cohort if a fourth patient was added and subsequently experienced a DLT. Additionally, text was inserted to specify that no DLTs were reported in the first 2 cohorts, and that therefore, the 2-week waiting period for cohort enrollment was removed from the study requirements. Text was also added to specify bone marrow aspirate/biopsy sample collection procedures for pharmacodynamic assessments and to clarify the process of determining the RP2D. Time points for the collection of blood samples used for PK and pharmacodynamic assessments and skin punch biopsies were added, as was guidance for the required Dose Escalation meeting required after 3 DLT-evaluable patients completed 1 cycle of treatment.
29 August 2014	The study design was changed to include EZH2 WT patients in 4 separate cohorts, with up to 30 patients allowed in each and early in-stream stopping criteria presented based on the response evaluation of 10 patients per cohort. A maximum feasible dose of 1600 mg was introduced, and 2 dose cohorts in the Dose Escalation part of the study were expanded to allow up to 12 patients each. A proposed dose of 200 mg was added for the FE part of the study.
14 October 2014	Bone marrow function requirements were streamlined and made less conservative. Additionally, text describing the timing of the pretreatment Screening period was corrected in the Schedule of Assessments and Procedures.

19 February 2015	Provided the rationale for the RP2D. A cohort of non-germinal-center B-cell-like subtype was included in Phase 2 and revised sample size estimate accordingly. Added details of on specific testing methods for EZH2 mutation and cell of origin for the phase 2 part of the study. Revised inclusion criteria for the phase 2 population to require that patients have R/R disease following at least 2 standard prior treatment regimens and have no curative options with other available therapy or those therapies are contraindicated. Objectives modified to remove clinical benefit rate, which is not a recognized efficacy measure in non-hodgkin lymphoma, and to add DOR, which has more clinical and regulatory relevance. Included an additional exploratory objective measurement of overall survival (OS) to be in line with existing protocol language on survival follow-up. Permitted clinically stable patients who had completed 6 cycles of therapy to have Day 15 assessment by telephone contact and local laboratory assessments. Following feedback from regulatory authorities, patients were no longer required to provide fresh tumor biopsies for the purpose of participation in this study. Modified the dose of tazemetostat to be used for the FE sub study to 400 mg. Requirement for skin punch biopsies was removed. Provided additional clarity that any dose interruption of over 28 days for any reason was to be discussed with the Medical Monitor. Stated the dose of tazemetostat in the DDI sub study as 800 mg. Added collection of anticancer therapies administered after tazemetostat.
21 May 2015	Protocol amended to allow for enrollment of patients ≥ 16 years of age in the FE and DDI sub studies.
15 September 2015	Updated the protocol due to acquisition of the clinical development for tazemetostat by Epizyme from Eisai. Simplified the protocol based on completion of Phase 1 (dose escalation and expansion and FE). Removed fasting restriction based on results of the FE study and included the tazemetostat could be administered with or without food. Added that patients who complete study-required assessments may participate in a rollover study. Updated dose modifications section. No longer required in-clinic visits on Day 15 after Cycle 2, only a telephone contact was required; patients were to have hematology and blood chemistry samples drawn at local laboratory. Changed radiologic tumor assessment to every 12 weeks after Cycle 6 to minimize radiation exposure and more accurately reflect standard of care. Changed screening brain magnetic resonance imaging to "only if clinically indicated". Added that all scans were to be submitted to the imaging core laboratory for quality assessment and archiving for potential independent review. Added the fluorodeoxyglucose-positron emission tomography should be conducted at first indication of CR or PR and that a repeat bone marrow biopsy should be performed at first indication of CR for patients with bone marrow involvement at screening. Modified physical exam to a symptom-directed exam during treatment period. Clarified that AEs and concomitant medications should be collected for 30 days after treatment discontinuation unless a new cancer therapy was started. Clarified the analyses to be conducted for PFS, DOR, and OS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The population PK data from this study were combined with PK data from other studies. The PK samples from the combination of tazemetostat with prednisolone were collected but not analyzed in this study.

Notes: