



Clinical trial results:

A Multicenter Open-Label Phase 1b/2 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Combination with Lenalidomide and Rituximab in Subjects with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Summary

EudraCT number	2013-004341-17
Trial protocol	BE GB
Global end of trial date	17 December 2020

Results information

Result version number	v1 (current)
This version publication date	16 December 2021
First version publication date	16 December 2021

Trial information

Trial identification

Sponsor protocol code	PCYC-1123-CA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02077166
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road,, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110 , abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110 , abbvieclinicaltrials@abbvie.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	17 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1b:

- To determine the maximum tolerated doses (MTD) and/or the recommended Phase 2 (RP2) dose of ibrutinib in combination with lenalidomide and rituximab by dose escalation of lenalidomide in subjects with relapsed or refractory DLBCL
- To determine the safety and tolerability of ibrutinib in combination with lenalidomide and rituximab in subjects with relapsed or refractory DLBCL by dose escalating lenalidomide

Phase 2:

- To evaluate the efficacy of ibrutinib in combination with lenalidomide and rituximab by assessing the overall response rate (ORR) in subjects with relapsed or refractory non-GCB DLBCL

Protection of trial subjects:

The Investigator or designee (designee must be listed on the Delegation of Authority log), must explain in terms understandable to the subject the purpose and nature of the study, study procedures, anticipated benefits, potential risks, possible adverse events (AEs), and any discomfort participation in the study may entail. This process must be documented in the subject's source record. Each subject must provide a signed and dated informed consent form (ICF) before any study-related (nonstandard of care) activities are performed.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 43
Country: Number of subjects enrolled	United States: 83
Worldwide total number of subjects	138
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	70
From 65 to 84 years	65
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

All participants had relapsed/refractory diffuse large B-cell lymphoma (DLBCL). In the Phase 1b portion of the study, all subtypes of DLBCL and participants with transformed disease were enrolled. In the Phase 2 portion of the study, only participants with non-germinal-center B-cell-like (non-GCB) DLBCL were enrolled.

Pre-assignment

Screening details:

In the Phase 1b portion of this study, different dose levels of lenalidomide were explored, and dose escalation of lenalidomide followed the 3+3+3 dose escalation schema.

Participants remained on study until disease progression or unacceptable toxicity. "Reason for non-completion" rows below display the primary reason for exiting the study.

Pre-assignment period milestones

Number of subjects started	138
Number of subjects completed	134

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not receive any treatment: 4
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Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)

Arm description:

Ibrutinib 560 mg administered orally (PO) once daily (QD) beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered intravenously (IV) on Day 1 of each 28-day cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm title	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level - 1)
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Arm description:

De-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 10 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
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Arm description:

Re-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm title	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
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Arm description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm title	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)
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Arm description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.	
Investigational medicinal product name	rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Arm title	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Arm description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Arm type	Experimental
Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Ibrutinib was administered orally daily beginning Cycle 1 Day 1.	
Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.	
Investigational medicinal product name	rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Arm title	Phase 2: Enrolled at Lenalidomide Dose 25 mg
Arm description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Arm type	Experimental

Investigational medicinal product name	ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ibrutinib was administered orally daily beginning Cycle 1 Day 1.

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide will be administered orally daily on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Rituximab was administered IV on Day 1 of each 28-day cycle for 6 cycles.

Number of subjects in period 1^[1]	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Started	12	7	9
Completed	0	0	0
Not completed	12	7	9
Consent withdrawn by subject	3	-	1
Study Closure by Sponsor	3	-	2
Death	6	7	5
Lost to follow-up	-	-	-
Other, Not Specified	-	-	1

Number of subjects in period 1^[1]	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Started	9	8	55
Completed	0	0	0
Not completed	9	8	55
Consent withdrawn by subject	1	1	3
Study Closure by Sponsor	2	2	12
Death	6	4	32
Lost to follow-up	-	-	1
Other, Not Specified	-	1	7

Number of subjects in period 1^[1]	Phase 2: Enrolled at Lenalidomide Dose 25 mg
Started	34
Completed	0
Not completed	34
Consent withdrawn by subject	-
Study Closure by Sponsor	4
Death	22
Lost to follow-up	-
Other, Not Specified	8

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 138 participants enrolled in the study; however, 4 participants exited the study without receiving any treatment, and are not presented in any data table.

Baseline characteristics

Reporting groups

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)
Reporting group description:	
Ibrutinib 560 mg administered orally (PO) once daily (QD) beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered intravenously (IV) on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)
Reporting group description:	
De-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 10 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Reporting group description:	
Re-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
Reporting group description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)
Reporting group description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Reporting group description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 25 mg
Reporting group description:	
Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	

Reporting group values	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Number of subjects	12	7	9
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	66.3 ± 13.13	58.4 ± 7.63	65.3 ± 13.44
Gender categorical Units: Subjects			
Female	4	3	5
Male	8	4	4
Ethnicity Units: Subjects			
Hispanic or Latino	1	3	1
Not Hispanic or Latino	11	4	8
Race Units: Subjects			
Asian	0	0	0
Black or African American	1	1	1
White	11	5	8
Multiple Races	0	0	0
Declined to Answer/ Unknown	0	1	0

Reporting group values	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Number of subjects	9	8	55
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	66.0 ± 8.63	62.9 ± 14.23	63.1 ± 11.75
Gender categorical Units: Subjects			
Female	5	3	23
Male	4	5	32
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	9	8	55
Race Units: Subjects			
Asian	0	0	1
Black or African American	0	1	2
White	9	7	51
Multiple Races	0	0	0
Declined to Answer/ Unknown	0	0	1

Reporting group values	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Total	
Number of subjects	34	134	

Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	64.9 ± 12.52	-	
Gender categorical Units: Subjects			
Female	14	57	
Male	20	77	
Ethnicity Units: Subjects			
Hispanic or Latino	5	10	
Not Hispanic or Latino	29	124	
Race Units: Subjects			
Asian	2	3	
Black or African American	1	7	
White	30	121	
Multiple Races	1	1	
Declined to Answer/ Unknown	0	2	

End points

End points reporting groups

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)
Reporting group description: Ibrutinib 560 mg administered orally (PO) once daily (QD) beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered intravenously (IV) on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level - 1)
Reporting group description: De-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 10 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Reporting group description: Re-escalation cohort: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
Reporting group description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)
Reporting group description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Reporting group description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 25 mg
Reporting group description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Subject analysis set title	All Phase 1b Participants
Subject analysis set type	Full analysis
Subject analysis set description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 10, 15, 20, or 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m ² administered IV on Day 1 of each 28-day cycle for 6 cycles.	
Subject analysis set title	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg
Subject analysis set type	Full analysis
Subject analysis set description: Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable	

toxicity. Lenalidomide 20 or 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Primary: Phase 1b: Recommended Phase 2 Dose of Lenalidomide in Combination With Fixed Doses of Ibrutinib and Rituximab in Participants With Relapsed or Refractory Diffuse Large B Cell Lymphoma (DLBCL)

End point title	Phase 1b: Recommended Phase 2 Dose of Lenalidomide in Combination With Fixed Doses of Ibrutinib and Rituximab in Participants With Relapsed or Refractory Diffuse Large B Cell Lymphoma (DLBCL) ^[1]
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End point description:

The dose levels of lenalidomide were explored, and dose escalation of lenalidomide followed the 3+3+3 dose escalation schema. A Dose Level Review Committee evaluated safety data following completion of each dose observation period of the Phase 1b portion.

All-Treated Analysis Population (Phase 1b): participants who received any dose of study drug(s).

End point type	Primary
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End point timeframe:

Estimated median time on study in Phase 1b was 59.6 months.

Notes:

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

Justification: Descriptive statistics are presented per protocol.

End point values	All Phase 1b Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: mg				
number (not applicable)	20			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, and Discontinuations Due to TEAEs

End point title	Phase 1b: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, and Discontinuations Due to TEAEs ^{[2][3]}
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End point description:

An adverse event (AE) is any untoward medical occurrence, which does not necessarily have a causal relationship with treatment. A serious AE is any untoward medical occurrence that at any dose: results in death; is life-threatening; requires in-patient hospitalization > 24 hours or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event. AEs that started or worsened during the treatment-emergent period and all possibly related or related AEs were considered TEAEs. Related events were those that were considered possibly related or related to study drug per investigator's judgment. Events were graded per the national Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.03: Grade 1=mild; grade 2=moderate; grade 3=severe; grade 4=life-threatening; grade 5=death.

All-Treated Analysis Population (Phase 1).

End point type	Primary
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End point timeframe:

From first dose of study drug up to 30 days after last dose of study drug. Phase 1b median duration of

ibrutinib exposure was 4.4 months; median duration of lenalidomide exposure was 4.4 months; median total number of doses of rituximab received was 4.0.

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: Descriptive statistics are presented per protocol.

[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: Phase 2 data are presented as a separate endpoint.

End point values	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	7	9	9
Units: participants				
TEAE	12	7	9	9
Grade ≥ 3 TEAE	11	6	9	9
Study Drug-Related TEAE	12	5	9	8
Grade ≥ 3 Study Drug-Related TEAE	10	3	8	7
Ibrutinib-Related TEAE	12	5	9	8
Grade ≥ 3 Ibrutinib-Related TEAE	10	3	7	7
Lenalidomide-Related TEAE	12	5	9	8
Grade ≥ 3 Lenalidomide-Related TEAE	9	3	8	7
Rituximab-Related TEAE	6	4	7	6
Grade ≥ 3 Rituximab-Related TEAE	1	2	7	5
TEAE Leading to Dose Reduction of Any Study Drug	4	0	4	4
TEAE Leading to Dose Reduction of Ibrutinib	3	0	4	3
TEAE Leading to Dose Reduction of Lenalidomide	2	0	3	4
TEAE Leading to Dose Delay of Any Study Drug	6	4	7	8
TEAE Leading to Dose Delay of Ibrutinib	6	4	7	8
TEAE Leading to Dose Delay of Lenalidomide	6	3	7	7
TEAE Leading to Dose Delay of Rituximab	4	1	6	4
TEAE Leading to Discontinuation of Any Study Drug	4	2	3	2
TEAE Leading to Discontinuation of Ibrutinib Dose	4	2	3	2
TEAE Leading to Discontinuation of Lenalid. Dose	4	2	3	2
TEAE Leading to Discontinuation of Rituximab Dose	3	2	3	2
Serious TEAE	4	6	7	5
Grade ≥ 3 Serious TEAE	4	6	6	4
Treatment-Related Serious TEAE	0	2	4	2
Ibrutinib-Related Serious TEAE	0	2	4	2
Lenalidomide-Related Serious TEAE	0	2	4	2
Rituximab-Related Serious TEAE	0	2	2	1
Fatal TEAE	0	2	2	1

End point values	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
TEAE	8			
Grade ≥ 3 TEAE	7			
Study Drug-Related TEAE	8			
Grade ≥ 3 Study Drug-Related TEAE	7			
Ibrutinib-Related TEAE	8			
Grade ≥ 3 Ibrutinib-Related TEAE	6			
Lenalidomide-Related TEAE	8			
Grade ≥ 3 Lenalidomide-Related TEAE	6			
Rituximab-Related TEAE	7			
Grade ≥ 3 Rituximab-Related TEAE	3			
TEAE Leading to Dose Reduction of Any Study Drug	5			
TEAE Leading to Dose Reduction of Ibrutinib	3			
TEAE Leading to Dose Reduction of Lenalidomide	4			
TEAE Leading to Dose Delay of Any Study Drug	8			
TEAE Leading to Dose Delay of Ibrutinib	8			
TEAE Leading to Dose Delay of Lenalidomide	8			
TEAE Leading to Dose Delay of Rituximab	4			
TEAE Leading to Discontinuation of Any Study Drug	1			
TEAE Leading to Discontinuation of Ibrutinib Dose	1			
TEAE Leading to Discontinuation of Lenalid. Dose	1			
TEAE Leading to Discontinuation of Rituximab Dose	1			
Serious TEAE	6			
Grade ≥ 3 Serious TEAE	6			
Treatment-Related Serious TEAE	3			
Ibrutinib-Related Serious TEAE	3			
Lenalidomide-Related Serious TEAE	3			
Rituximab-Related Serious TEAE	0			
Fatal TEAE	1			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall Response Rate (ORR)

End point title	Phase 2: Overall Response Rate (ORR) ^{[4][5]}
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End point description:

The ORR was defined as the percentage of participants who achieve either a partial response (PR) or complete response (CR), according to the Revised International Working Group Response Criteria for Malignant Lymphoma or Lugano Classification (see Cheson, 2014 for detailed criteria), as assessed by the investigator in response-evaluable population. The 95% confidence interval (CI) was calculated using the exact method.

Response-Evaluable Population: participants who had measurable disease at baseline and had at least 1 adequate post-treatment disease assessment by the investigator.

End point type	Primary
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End point timeframe:

Estimated median time on study in Phase 2 was 35.0 months.

Notes:

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

Justification: Descriptive statistics are presented per protocol.

[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: Phase 1 data are presented as a separate endpoint.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	32	85	
Units: percentage of participants				
number (confidence interval 95%)	52.8 (38.6 to 66.7)	43.8 (26.4 to 62.3)	49.4 (38.4 to 60.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: ORR

End point title	Phase 1b: ORR ^[6]
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End point description:

The ORR was defined as the percentage of participants who achieve either a PR or CR, according to the Revised International Working Group Response Criteria for Malignant Lymphoma (Cheson 2007), as assessed by the Investigator in response-evaluable population, where CR=disappearance of all evidence of disease and PR=regression of measurable disease and no new sites. The 95% CI was calculated using the exact method.

Response-Evaluable Population: participants who had measurable disease at baseline and had at least 1 adequate post-treatment disease assessment by the investigator.

End point type	Secondary
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End point timeframe:

Estimated median time on study in Phase 1b was 59.6 months.

Notes:

[6] - 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: Phase 2 data are presented as a separate endpoint.

End point values	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	7	9
Units: percentage of participants				
number (confidence interval 95%)	44.4 (13.7 to 78.8)	0 (0 to 41.0)	71.4 (29.0 to 96.3)	22.2 (2.8 to 60.0)

End point values	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	All Phase 1b Participants		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	8	40		
Units: percentage of participants				
number (confidence interval 95%)	75.0 (34.9 to 96.8)	42.5 (27.0 to 59.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Complete Response (CR) Rate

End point title	Phase 1b: Complete Response (CR) Rate ^[7]
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End point description:

The CR rate was defined as the percentage of participants who achieve a CR, according to the Revised International Working Group Response Criteria for Malignant Lymphoma (Cheson 2007), as assessed by the Investigator in response-evaluable population, where CR=disappearance of all evidence of disease, as assessed by the Investigator.

Response-Evaluable Population: participants who had measurable disease at baseline and had at least 1 adequate post-treatment disease assessment by the investigator.

End point type	Secondary
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End point timeframe:

Estimated median time on Phase 1b study was 59.6 months.

Notes:

[7] - 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: Phase 2 data are presented as a separate endpoint.

End point values	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	7	9
Units: percentage of participants				
number (not applicable)	33.3	0	42.9	11.1

End point values	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	All Phase 1b Participants		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	8	40		
Units: percentage of participants				
number (not applicable)	50.0	27.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: CR Rate

End point title	Phase 2: CR Rate ^[8]
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End point description:

The CR rate was defined as the percentage of participants who achieve a CR, according to the Revised International Working Group Response Criteria for Malignant Lymphoma or Lugano Classification (see Cheson, 2014 for detailed criteria), as assessed by the Investigator in response-evaluable population.

Response-Evaluable Population: participants who had measurable disease at baseline and had at least 1 adequate post-treatment disease assessment by the investigator.

End point type	Secondary
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End point timeframe:

Estimated median time on study in Phase 2 was 35.0 months.

Notes:

[8] - 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: Phase 1 data are presented as a separate endpoint.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	32	89	
Units: percentage of participants				
number (not applicable)	32.1	21.9	28.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR) ^[9]
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End point description:

DOR is defined as the time from the date of the first documented response (CR or PR) to the first documented evidence of disease progression (PD) according to the Revised International Working Group Response Criteria for Malignant Lymphoma or Lugano Classification (Cheson 2014) or death from any cause. For participants who had achieved an overall response but did not die or progress at the time of analysis, DOR was censored on the date of the last adequate post-baseline disease assessment, or on the date of the first occurrence of response (CR or PR) if there was no disease assessment afterwards. 2-sided 95% CI is estimated by Kaplan-Meier method.

All-Treated Analysis Population (Phase 2): participants who received any dose of study drug(s). Participants who achieved Overall Response.

End point type	Secondary
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End point timeframe:

Estimated median time on study in Phase 2 was 35.0 months.

Notes:

[9] - 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: Per protocol, this endpoint addresses Phase 2 only.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28 ^[10]	14	42 ^[11]	
Units: months				
median (confidence interval 95%)	38.3 (3.7 to 99999)	28.6 (2.8 to 28.6)	38.3 (9.5 to 99999)	

Notes:

[10] - 99999=The 95% Confidence limit cannot be estimated.

[11] - 99999=The 95% Confidence limit cannot be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression Free Survival (PFS)

End point title	Phase 2: Progression Free Survival (PFS) ^[12]
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End point description:

PFS is defined as the time from the date of the first dose of study drug to confirmed PD according to the Revised International Working Group Response Criteria for Malignant Lymphoma or Lugano Classification (Cheson 2014) or death from any cause, whichever occurred first. For participants without disease progression or death, PFS data was censored at the date of the last tumor assessment. 2 sided 95% CI is estimated by Kaplan-Meier method.

All-Treated Analysis Population (Phase 2): participants who received any dose of study drug(s).

End point type	Secondary
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End point timeframe:

Estimated median time on study in Phase 2 was 35.0 months.

Notes:

[12] - 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: Per protocol, this endpoint addresses Phase 2 only.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	55	34	89	
Units: months				
median (confidence interval 95%)	5.4 (3.4 to 11.3)	4.7 (2.6 to 24.8)	5.4 (3.4 to 6.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS) ^[13]
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End point description:

OS is defined as the time from the date of the first dose of study drug to the date of death due to any cause. For participants not known to have died at or prior to the database lock date, OS data was censored at the date last known alive. Participants who withdrew consent prior to study closure were censored on the date of the consent withdrawal. 2-sided 95% CI was estimated by Kaplan-Meier method.

All-Treated Analysis Population (Phase 2): participants who received any dose of study drug(s).

End point type	Secondary
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End point timeframe:

Estimated median time on study in Phase 2 was 35.0 months.

Notes:

[13] - 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: Per protocol, this endpoint addresses Phase 2 only.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	55	34 ^[14]	89	
Units: months				
median (confidence interval 95%)	14.7 (9.7 to 32.8)	11.6 (5.7 to 99999)	14.2 (9.7 to 28.1)	

Notes:

[14] - 99999=The 95% Confidence limit cannot be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With TEAEs, Serious TEAEs, and Discontinuations Due to TEAEs

End point title	Phase 2: Number of Participants With TEAEs, Serious TEAEs, and Discontinuations Due to TEAEs ^[15]
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End point description:

An AE is any untoward medical occurrence, which does not necessarily have a causal relationship with treatment. A serious AE is any untoward medical occurrence that at any dose: results in death; is life-threatening; requires in-patient hospitalization > 24 hours or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event. AEs that started or worsened during the treatment-emergent period and all possibly related or related AEs were considered TEAEs. Related events were those that were considered possibly related or related to study drug per investigator's judgment. Events were graded per the national Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.03: Grade 1=mild; grade 2=moderate; grade 3=severe; grade 4=life-threatening; grade 5=death.

All-Treated Analysis Population (Phase 2): participants who received any dose of study drug(s).

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 30 days after last dose of study drug. Phase 2 median duration of ibrutinib exposure=4.9 months; median duration of lenalidomide exposure=4.7 months; median total number of doses of rituximab received=5.0.

Notes:

[15] - 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: Phase 1 data are presented as a separate endpoint.

End point values	Phase 2: Enrolled at Lenalidomide Dose 20 mg	Phase 2: Enrolled at Lenalidomide Dose 25 mg	Phase 2 Total: Enrolled at Lenalidomide Dose 20 or 25 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	55	34	89	
Units: participants				
TEAE	55	34	89	
Grade ≥3 TEAE	51	30	81	
Study Drug-Related TEAE	52	33	85	
Grade ≥3 Study Drug-Related TEAE	41	25	66	
Ibrutinib-Related TEAE	50	32	82	
Grade ≥3 Ibrutinib-Related TEAE	36	24	60	
Lenalidomide-Related TEAE	51	32	83	
Grade ≥3 Lenalidomide-Related TEAE	40	25	65	
Rituximab-Related TEAE	37	25	62	
Grade ≥3 Rituximab-Related TEAE	18	13	31	
TEAE Leading to Dose Reduction of Any Study Drug	23	14	37	

TEAE Leading to Dose Reduction of Ibrutinib	12	9	21	
TEAE Leading to Dose Reduction of Lenalidomide	21	14	35	
TEAE Leading to Dose Delay of Any Study Drug	40	29	69	
TEAE Leading to Dose Delay of Ibrutinib	38	28	66	
TEAE Leading to Dose Delay of Lenalidomide	37	26	63	
TEAE Leading to Dose Delay of Rituximab	10	6	16	
TEAE Leading to Discontinuation of Any Study Drug	11	7	18	
TEAE Leading to Discontinuation of Ibrutinib Dose	11	5	16	
TEAE Leading to Discontinuation of Lenalid. Dose	11	7	18	
TEAE Leading to Discontinuation of Rituximab Dose	6	4	10	
Serious TEAE	32	25	57	
Grade ≥ 3 Serious TEAE	29	21	50	
Treatment-Related Serious TEAE	16	12	28	
Ibrutinib-Related Serious TEAE	14	12	26	
Lenalidomide-Related Serious TEAE	16	10	26	
Rituximab-Related Serious TEAE	4	5	9	
Fatal TEAE	8	4	12	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 30 days after last dose of study drug. Phase 1b median duration of ibrutinib exposure was 4.4 months; median duration of lenalidomide exposure was 4.4 months; median total number of doses of rituximab received was 4.0

Adverse event reporting additional description:

Phase 2 median duration of ibrutinib exposure was 4.9 months; median duration of lenalidomide exposure was 4.7 months; median total number of doses of rituximab received was 5.0.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level - 1)
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 10 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 15 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 20 mg
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 20 mg administered PO QD on Days 1-21 of each 28-day cycle until disease progression or unacceptable toxicity. Rituximab 375 mg/m² administered IV on Day 1 of each 28-day cycle for 6 cycles.

Reporting group title	Phase 2: Enrolled at Lenalidomide Dose 25 mg
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Reporting group description:

Ibrutinib 560 mg administered PO QD beginning Cycle 1 Day 1 until disease progression or unacceptable toxicity. Lenalidomide 25 mg administered PO QD on Days 1-21 of each 28-day cycle until disease

Serious adverse events	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	6 / 7 (85.71%)	7 / 9 (77.78%)
number of deaths (all causes)	7	7	5
number of deaths resulting from adverse events	0	2	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIFFUSE LARGE B-CELL LYMPHOMA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG NEOPLASM MALIGNANT			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCULAR LYMPHOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER SITE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (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
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
PROSTATIC OBSTRUCTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSпноEA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
PLEURISY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 NECK FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (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
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
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 FLUTTER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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			
DIZZINESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLIC CEREBRAL INFARCTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYTIC ANAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

COLITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROSPLENIC FISTULA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER ENLARGEMENT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PURPURA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDRONEPHROSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 OBSTRUCTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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			
ARTHRALGIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOBILITY DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 OSTEOARTHRITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 ACUTE SINUSITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
BRONCHITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
CANDIDA INFECTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
CELLULITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	1 / 7 (14.29%) 1 / 1 0 / 0	1 / 9 (11.11%) 2 / 3 0 / 0
CELLULITIS ORBITAL subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
ESCHERICHIA SEPSIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	1 / 9 (11.11%) 1 / 1 1 / 1
FOLLICULITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	1 / 7 (14.29%) 1 / 1 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
HAEMATOMA INFECTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 12 (0.00%) 0 / 0 0 / 0	0 / 7 (0.00%) 0 / 0 0 / 0	0 / 9 (0.00%) 0 / 0 0 / 0
INFLUENZA			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 BACTERIAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHANGITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA VIRAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLA BACTERAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
SEPSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND SEPSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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			
DEHYDRATION			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAILURE TO THRIVE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
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 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 9 (55.56%)	6 / 8 (75.00%)	32 / 55 (58.18%)
number of deaths (all causes)	7	5	33
number of deaths resulting from adverse events	1	1	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIFFUSE LARGE B-CELL LYMPHOMA			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 4
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCULAR LYMPHOMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER SITE PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
FATIGUE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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

PYREXIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
PROSTATIC OBSTRUCTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COUGH			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (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
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDAL IDEATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
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 NECK FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	3 / 3	3 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLIC CEREBRAL INFARCTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYTIC ANAEMIA			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 UPPER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC HAEMORRHAGE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROSPLENIC FISTULA			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
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	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (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
NAUSEA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER ENLARGEMENT			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
PURPURA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (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
HYDRONEPHROSIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOBILITY DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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			
ACUTE SINUSITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CANDIDA INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
CELLULITIS			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS ORBITAL			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOLLICULITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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 BACTERIAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHANGITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA VIRAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLA BACTERAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
SEPTIC SHOCK			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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	1 / 9 (11.11%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND SEPSIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAILURE TO THRIVE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCALCAEMIA			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (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
TUMOUR LYSIS SYNDROME			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
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: Enrolled at Lenalidomide Dose 25 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 34 (73.53%)		
number of deaths (all causes)	22		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
BOWEN'S DISEASE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
DIFFUSE LARGE B-CELL LYMPHOMA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LUNG NEOPLASM MALIGNANT			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OCULAR LYMPHOMA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOTENSION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CATHETER SITE PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

CHILLS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FATIGUE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYREXIA			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
PROSTATIC OBSTRUCTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COUGH			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DYSPNOEA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PLEURAL EFFUSION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PLEURISY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CONFUSIONAL STATE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DELIRIUM			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUICIDAL IDEATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FIBULA FRACTURE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
ATRIAL FLUTTER			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
EMBOLIC CEREBRAL INFARCTION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

SYNCOPE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FEBRILE NEUTROPENIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
HAEMOLYTIC ANAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PANCYTOPENIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

COLITIS				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GASTRIC HAEMORRHAGE				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROSPLENIC FISTULA				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
INCARCERATED INGUINAL HERNIA				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INTESTINAL OBSTRUCTION				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NAUSEA				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SMALL INTESTINAL OBSTRUCTION				

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VOMITING			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GALLBLADDER ENLARGEMENT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PURPURA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYDRONEPHROSIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BACK PAIN			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MOBILITY DECREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations ACUTE SINUSITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
BRONCHITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
CANDIDA INFECTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
CELLULITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 34 (2.94%) 1 / 1 0 / 0		
CELLULITIS ORBITAL subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
ESCHERICHIA SEPSIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
FOLLICULITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
HAEMATOMA INFECTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 34 (0.00%) 0 / 0 0 / 0		
INFLUENZA			

subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION BACTERIAL				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
LYMPHANGITIS				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIC SEPSIS				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PARAINFLUENZAE VIRUS INFECTION				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERITONITIS				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	2 / 34 (5.88%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
PNEUMONIA BACTERIAL				

subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA VIRAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SALMONELLA BACTERAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEPSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEPTIC SHOCK			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
WOUND SEPSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DEHYDRATION			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FAILURE TO THRIVE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERCALCAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPONATRAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1)	Phase 1b: Enrolled at Lenalidomide Dose 10 mg (Dose Level -1)	Phase 1b: Enrolled at Lenalidomide Dose 15 mg (Dose Level 1+)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	7 / 7 (100.00%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
LIPOMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
TUMOUR PAIN			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	1 / 9 (11.11%) 1
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HOT FLUSH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
HYPOTENSION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	2
PERIPHERAL COLDNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VARICOSE VEIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ADVERSE DRUG REACTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ASTHENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	2
CHEST DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CHILLS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	3
FACE OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	6 / 12 (50.00%)	3 / 7 (42.86%)	5 / 9 (55.56%)
occurrences (all)	8	3	9
GAIT DISTURBANCE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFUSION SITE SWELLING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
INJECTION SITE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MALAISE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
NODULE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	3 / 9 (33.33%)
occurrences (all)	2	1	3
PAIN			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 7 (28.57%) 2	2 / 9 (22.22%) 2
PERIPHERAL SWELLING subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
PYREXIA subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 2	2 / 9 (22.22%) 4
VESSEL PUNCTURE SITE BRUISE subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
HYPERSENSITIVITY subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
HYPOGAMMAGLOBULINAEMIA subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
SEASONAL ALLERGY subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
Social circumstances PHYSICAL ASSAULT subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
Reproductive system and breast disorders GENITAL RASH subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
OEDEMA GENITAL subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	0 / 9 (0.00%) 0
VAGINAL HAEMORRHAGE			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
ALLERGIC SINUSITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
APHONIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	3 / 12 (25.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	3	0	4
DYSPHONIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DYSPNOEA			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	2	3	2
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
EPISTAXIS			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	4	1	0
HICCUPS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
HYPOXIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LUNG DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			

subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
NASAL DRYNESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
NASAL SEPTUM PERFORATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PNEUMONITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
RESPIRATORY DISORDER			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RHINORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	3

SINUS CONGESTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
WHEEZING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
YAWNING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
DEPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DISORIENTATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
INSOMNIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
IRRITABILITY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
STRESS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BLOOD URINE PRESENT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
BODY TEMPERATURE FLUCTUATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	3
CREATININE RENAL CLEARANCE DECREASED			

subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	2
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCUS TEST POSITIVE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
VITAMIN D DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	2 / 12 (16.67%)	2 / 7 (28.57%)	2 / 9 (22.22%)
occurrences (all)	2	2	2
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
EYE CONTUSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FALL			

subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
IMPACTED FRACTURE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MOUTH INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
NAIL INJURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
POST PROCEDURAL HAEMATOMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RIB FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SCRATCH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SKIN ABRASION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN LACERATION			

subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
WOUND			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
PALPITATIONS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
TACHYCARDIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ATAXIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BALANCE DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			

subjects affected / exposed	4 / 12 (33.33%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	5	0	2
DIZZINESS POSTURAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSARTHRIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
DYSGEUSIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HEAD DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	2	0	3
HYPOAESTHESIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
PARAESTHESIA			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
PARKINSON'S DISEASE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORIMOTOR NEUROPATHY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	1	0

PRESYNCOPE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SCIATICA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SPEECH DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
TREMOR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 12 (33.33%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	6	0	6
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	3	1	3
LEUKOCYTOSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	7	0	0
LYMPHADENOPATHY			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
LYMPHOCYTOSIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LYMPHOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
NEUTROPENIA			
subjects affected / exposed	5 / 12 (41.67%)	0 / 7 (0.00%)	6 / 9 (66.67%)
occurrences (all)	13	0	46
PANCYTOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 12 (33.33%)	2 / 7 (28.57%)	4 / 9 (44.44%)
occurrences (all)	8	5	9
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
EAR PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
HYPOACUSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CATARACT			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CHALAZION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
DRY AGE-RELATED MACULAR DEGENERATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DRY EYE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
EXOPHTHALMOS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EYE OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EYE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EYE PRURITUS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
METAMORPHOPSIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OCULAR HYPERAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
OPTIC NERVE COMPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

PERIORBITAL SWELLING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
PHOTOPHOBIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TRICHIASIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VISUAL ACUITY REDUCED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
ABDOMINAL DISTENSION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
ABDOMINAL PAIN			
subjects affected / exposed	2 / 12 (16.67%)	2 / 7 (28.57%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
CONSTIPATION			
subjects affected / exposed	5 / 12 (41.67%)	2 / 7 (28.57%)	4 / 9 (44.44%)
occurrences (all)	5	2	4
DEFAECATION URGENCY			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	9 / 12 (75.00%)	3 / 7 (42.86%)	3 / 9 (33.33%)
occurrences (all)	22	4	3
DRY MOUTH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FAECES DISCOLOURED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FLATULENCE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
GASTRITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
GINGIVAL BLEEDING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
GINGIVAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GINGIVAL SWELLING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

GLOSSODYNIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAEMATEMESIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
HYPERCHLORHYDRIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MELAENA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MOUTH ULCERATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
subjects affected / exposed	7 / 12 (58.33%)	3 / 7 (42.86%)	3 / 9 (33.33%)
occurrences (all)	10	4	4
ORAL DISORDER			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ORAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

STOMATITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
TONGUE ULCERATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
TOOTH LOSS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
TOOTHACHE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	3 / 12 (25.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	3	1	1
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HEPATIC CYST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
HEPATOMEGALY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ACTINIC KERATOSIS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLISTER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLOOD BLISTER			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
DRY SKIN			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ECCHYMOSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
HYPERHIDROSIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
INGROWING NAIL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
MACULE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
NIGHT SWEATS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
ONYCHOCLASIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
PETECHIAE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PRURITUS			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
PURPURA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RASH			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RASH ERYTHEMATOUS			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
RASH MACULAR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RASH MACULO-PAPULAR			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	5 / 9 (55.56%)
occurrences (all)	5	2	11
RASH PRURITIC			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SCAB			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SKIN DISCOLOURATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN EXFOLIATION			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN FISSURES			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SKIN HYPERPIGMENTATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SKIN IRRITATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN LESION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
STASIS DERMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Renal and urinary disorders			
BLADDER TRABECULATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSURIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URETHRAL STENOSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

URINARY RETENTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	4 / 12 (33.33%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	4	0	4
BACK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	3 / 9 (33.33%)
occurrences (all)	0	1	4
BONE PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FLANK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
GROIN PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MUSCLE ATROPHY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	2	2	3
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
NECK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
OSTEOARTHRITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	2	1	5
PAIN IN JAW			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RHABDOMYOLYSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLISTER INFECTED			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

BRONCHITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CHRONIC SINUSITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CLOSTRIDIUM COLITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
CONJUNCTIVITIS BACTERIAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CORONAVIRUS INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CYSTITIS KLEBSIELLA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
EYE INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FOLLICULITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FURUNCLE			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
HERPES ZOSTER			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
IMPETIGO			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NAIL INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OTITIS EXTERNA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OTITIS MEDIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PNEUMONIA			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PSEUDOMONAS INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PUSTULE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RASH PUSTULAR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	2	2	2
SINUSITIS BACTERIAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
TINEA PEDIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	2
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
WOUND ABSCESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
WOUND INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
WOUND INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	4 / 9 (44.44%)
occurrences (all)	2	1	7
DEHYDRATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ENZYME ABNORMALITY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPERCALCAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	6
HYPERKALAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	7	0	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			

subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPOCALCAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
HYPOKALAEMIA			
subjects affected / exposed	4 / 12 (33.33%)	1 / 7 (14.29%)	3 / 9 (33.33%)
occurrences (all)	8	1	7
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	4
HYPONATRAEMIA			
subjects affected / exposed	3 / 12 (25.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	4	0	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MALNUTRITION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Non-serious adverse events	Phase 1b: Enrolled at Lenalidomide Dose 20 mg (Dose Level 2)	Phase 1b: Enrolled at Lenalidomide Dose 25 mg (Dose Level 3)	Phase 2: Enrolled at Lenalidomide Dose 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	8 / 8 (100.00%)	54 / 55 (98.18%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
LIPOMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
HOT FLUSH			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	3	21
HYPOTENSION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
PERIPHERAL COLDNESS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
VARICOSE VEIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ADVERSE DRUG REACTION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
ASTHENIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	1 / 55 (1.82%)
occurrences (all)	0	2	2
CHEST DISCOMFORT			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	2	0	1
CHEST PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	2
CHILLS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
FACE OEDEMA			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	2 / 9 (22.22%)	3 / 8 (37.50%)	22 / 55 (40.00%)
occurrences (all)	3	4	34
GAIT DISTURBANCE			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	1	1	2
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
INFUSION SITE SWELLING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE PAIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
MALAISE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	0	4	3
NODULE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
OEDEMA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 9 (33.33%)	4 / 8 (50.00%)	21 / 55 (38.18%)
occurrences (all)	3	5	30
PAIN			
subjects affected / exposed	0 / 9 (0.00%)	3 / 8 (37.50%)	2 / 55 (3.64%)
occurrences (all)	0	3	2
PERIPHERAL SWELLING			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	4 / 55 (7.27%) 5
PYREXIA subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	3 / 8 (37.50%) 3	2 / 55 (3.64%) 2
VESSEL PUNCTURE SITE BRUISE subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	0 / 55 (0.00%) 0
HYPERSENSITIVITY subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	0 / 55 (0.00%) 0
HYPOGAMMAGLOBULINAEMIA subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	3 / 55 (5.45%) 3
SEASONAL ALLERGY subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	2 / 8 (25.00%) 2	0 / 55 (0.00%) 0
Social circumstances PHYSICAL ASSAULT subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
Reproductive system and breast disorders GENITAL RASH subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
OEDEMA GENITAL subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
VAGINAL HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	0 / 55 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

ALLERGIC SINUSITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
APHONIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
COUGH			
subjects affected / exposed	0 / 9 (0.00%)	3 / 8 (37.50%)	18 / 55 (32.73%)
occurrences (all)	0	5	27
DYSPHONIA			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	2	1	2
DYSPNOEA			
subjects affected / exposed	3 / 9 (33.33%)	3 / 8 (37.50%)	17 / 55 (30.91%)
occurrences (all)	3	3	23
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences (all)	0	0	7
EPISTAXIS			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences (all)	2	0	7
HICCUPS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
HYPOXIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
LUNG DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
NASAL CONGESTION			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	4 / 55 (7.27%)
occurrences (all)	1	1	5
NASAL DRYNESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0

NASAL SEPTUM PERFORATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	6 / 55 (10.91%)
occurrences (all)	1	1	9
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
PLEURAL EFFUSION			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	4 / 55 (7.27%)
occurrences (all)	0	4	7
PNEUMONITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 9 (11.11%)	3 / 8 (37.50%)	4 / 55 (7.27%)
occurrences (all)	1	3	6
RESPIRATORY DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
RHINORRHOEA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	4 / 55 (7.27%)
occurrences (all)	0	4	4
SINUS CONGESTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT CONGESTION			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
WHEEZING			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
YAWNING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
CONFUSIONAL STATE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
DISORIENTATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences (all)	0	1	5
IRRITABILITY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
STRESS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	1	2	3
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	3
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	3
BLOOD CREATINE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	8
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BODY TEMPERATURE FLUCTUATION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	4
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	1 / 9 (11.11%)	3 / 8 (37.50%)	6 / 55 (10.91%)
occurrences (all)	1	3	11
LYMPHOCYTE COUNT DECREASED			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	4	2
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	7 / 55 (12.73%)
occurrences (all)	0	7	53
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences (all)	0	1	14
STAPHYLOCOCCUS TEST POSITIVE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	2	0	1
VITAMIN D DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
WEIGHT DECREASED			
subjects affected / exposed	1 / 9 (11.11%)	3 / 8 (37.50%)	8 / 55 (14.55%)
occurrences (all)	1	3	11
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	6 / 55 (10.91%)
occurrences (all)	0	1	7
EYE CONTUSION			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
FALL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
IMPACTED FRACTURE			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
LIMB INJURY			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
MOUTH INJURY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
NAIL INJURY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL HAEMATOMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
RIB FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
SCRATCH			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
SKIN ABRASION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
SKIN LACERATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
WOUND			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	5	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	2
PALPITATIONS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
ATAXIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BALANCE DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
DIZZINESS			
subjects affected / exposed	3 / 9 (33.33%)	1 / 8 (12.50%)	11 / 55 (20.00%)
occurrences (all)	5	2	16
DIZZINESS POSTURAL			

subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
DYSARTHRIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	4
HEAD DISCOMFORT			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
HEADACHE			
subjects affected / exposed	1 / 9 (11.11%)	3 / 8 (37.50%)	3 / 55 (5.45%)
occurrences (all)	1	3	4
HYPOAESTHESIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
PARAESTHESIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences (all)	0	1	5
PARKINSON'S DISEASE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	6
PERIPHERAL SENSORIMOTOR NEUROPATHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	11 / 55 (20.00%)
occurrences (all)	1	1	20
PRESYNCOPE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1

RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
SCIATICA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
SPEECH DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
SYNCOPE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	2
TREMOR			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	4 / 55 (7.27%)
occurrences (all)	2	1	4
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 9 (33.33%)	2 / 8 (25.00%)	17 / 55 (30.91%)
occurrences (all)	22	6	88
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	8 / 55 (14.55%)
occurrences (all)	0	2	13
LEUKOCYTOSIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
LEUKOPENIA			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	4	2	35
LYMPHADENOPATHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
LYMPHOCYTOSIS			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	0 / 55 (0.00%) 0
LYMPHOPENIA			
subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	0 / 8 (0.00%) 0	0 / 55 (0.00%) 0
NEUTROPENIA			
subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 22	5 / 8 (62.50%) 41	25 / 55 (45.45%) 126
PANCYTOPENIA			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
SPONTANEOUS HAEMATOMA			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	2 / 55 (3.64%) 2
THROMBOCYTOPENIA			
subjects affected / exposed occurrences (all)	4 / 9 (44.44%) 21	3 / 8 (37.50%) 10	11 / 55 (20.00%) 61
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	1 / 55 (1.82%) 1
EAR PAIN			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	1 / 55 (1.82%) 1
HYPOACUSIS			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	1 / 55 (1.82%) 1
VERTIGO			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	0 / 55 (0.00%) 0
Eye disorders			
CATARACT			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0	2 / 55 (3.64%) 3
CHALAZION			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
DRY AGE-RELATED MACULAR DEGENERATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
DRY EYE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	6 / 55 (10.91%)
occurrences (all)	1	0	7
EXOPHTHALMOS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
EYE OEDEMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
EYE PAIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
EYE PRURITUS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	4
METAMORPHOPSIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
OPTIC NERVE COMPRESSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL SWELLING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0

PHOTOPHOBIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
TRICHIASIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
VISION BLURRED			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	1	1	2
VISUAL ACUITY REDUCED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	1	1	2
ABDOMINAL PAIN			
subjects affected / exposed	3 / 9 (33.33%)	2 / 8 (25.00%)	9 / 55 (16.36%)
occurrences (all)	3	2	11
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	4
CONSTIPATION			
subjects affected / exposed	4 / 9 (44.44%)	3 / 8 (37.50%)	11 / 55 (20.00%)
occurrences (all)	4	5	17
DEFAECATION URGENCY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
DIARRHOEA			

subjects affected / exposed	4 / 9 (44.44%)	7 / 8 (87.50%)	32 / 55 (58.18%)
occurrences (all)	8	16	83
DRY MOUTH			
subjects affected / exposed	1 / 9 (11.11%)	2 / 8 (25.00%)	8 / 55 (14.55%)
occurrences (all)	1	2	9
DYSPEPSIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	7 / 55 (12.73%)
occurrences (all)	0	2	7
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
FAECES DISCOLOURED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
FLATULENCE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences (all)	0	1	9
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
GINGIVAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
GINGIVAL SWELLING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
GLOSSODYNIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1

HAEMATEMESIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
HAEMORRHOIDS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
HYPERCHLORHYDRIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
MELAENA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
MOUTH ULCERATION			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	2	0	1
NAUSEA			
subjects affected / exposed	3 / 9 (33.33%)	4 / 8 (50.00%)	17 / 55 (30.91%)
occurrences (all)	5	8	20
ORAL DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	3 / 8 (37.50%)	4 / 55 (7.27%)
occurrences (all)	0	3	4
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	7 / 55 (12.73%)
occurrences (all)	2	1	7

TONGUE ULCERATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
TOOTH LOSS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	3 / 9 (33.33%)	2 / 8 (25.00%)	12 / 55 (21.82%)
occurrences (all)	6	3	19
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
HEPATIC CYST			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
HEPATOMEGALY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
ACTINIC KERATOSIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
BLISTER			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BLOOD BLISTER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
DERMATITIS CONTACT			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	13 / 55 (23.64%)
occurrences (all)	1	1	15
ECCHYMOSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
ECZEMA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
ERYTHEMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	6 / 55 (10.91%)
occurrences (all)	0	0	9
HYPERHIDROSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
INGROWING NAIL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
MACULE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	4 / 55 (7.27%)
occurrences (all)	1	0	9
ONYCHOCLASIS			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
PETECHIAE			
subjects affected / exposed	4 / 9 (44.44%)	2 / 8 (25.00%)	5 / 55 (9.09%)
occurrences (all)	5	3	10
PRURITUS			
subjects affected / exposed	3 / 9 (33.33%)	0 / 8 (0.00%)	7 / 55 (12.73%)
occurrences (all)	3	0	11
PURPURA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences (all)	0	0	5
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	4 / 55 (7.27%)
occurrences (all)	0	2	4
RASH MACULAR			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	7 / 55 (12.73%)
occurrences (all)	0	0	11
RASH MACULO-PAPULAR			
subjects affected / exposed	3 / 9 (33.33%)	2 / 8 (25.00%)	15 / 55 (27.27%)
occurrences (all)	5	3	40
RASH PRURITIC			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	2
SCAB			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
SKIN EXFOLIATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
SKIN FISSURES			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	4
SKIN HYPERPIGMENTATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
SKIN IRRITATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
SKIN LESION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
STASIS DERMATITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
BLADDER TRABECULATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
DYSURIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
HAEMATURIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	1	2	11
URETHRAL STENOSIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
URINARY INCONTINENCE			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	1	2	0
URINARY RETENTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1

Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 9 (22.22%)	2 / 8 (25.00%)	9 / 55 (16.36%)
occurrences (all)	4	2	12
BACK PAIN			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	10 / 55 (18.18%)
occurrences (all)	0	4	12
BONE PAIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	2	3
FLANK PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
GROIN PAIN			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
JOINT SWELLING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences (all)	0	0	5
MUSCLE ATROPHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 9 (0.00%)	3 / 8 (37.50%)	12 / 55 (21.82%)
occurrences (all)	0	3	18
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	1	1	2
MUSCULOSKELETAL DISCOMFORT			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	5
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	4 / 55 (7.27%)
occurrences (all)	1	0	4
MYALGIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	4 / 55 (7.27%)
occurrences (all)	0	4	8
NECK PAIN			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
OSTEOARTHRITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	5 / 55 (9.09%)
occurrences (all)	1	1	5
PAIN IN JAW			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
RHABDOMYOLYSIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BLISTER INFECTED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3

CHRONIC SINUSITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
CLOSTRIDIUM COLITIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	4 / 55 (7.27%)
occurrences (all)	2	1	4
CONJUNCTIVITIS BACTERIAL			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
CORONAVIRUS INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
CYSTITIS KLEBSIELLA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
EYE INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
FOLLICULITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
FURUNCLE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
GASTROENTERITIS VIRAL			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
HERPES ZOSTER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
IMPETIGO			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
INFLUENZA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
NAIL INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
NASOPHARYNGITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	7 / 55 (12.73%)
occurrences (all)	0	0	10
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
OTITIS EXTERNA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
PHARYNGITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
PNEUMONIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	2 / 55 (3.64%)
occurrences (all)	0	2	3
PSEUDOMONAS INFECTION			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
PUSTULE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
RASH PUSTULAR			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	1	7
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
SINUSITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	4 / 55 (7.27%)
occurrences (all)	0	2	5
SINUSITIS BACTERIAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
TINEA PEDIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	12 / 55 (21.82%)
occurrences (all)	0	9	22
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 9 (11.11%)	3 / 8 (37.50%)	7 / 55 (12.73%)
occurrences (all)	1	3	8
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
WOUND ABSCESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
WOUND INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
WOUND INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 9 (22.22%)	2 / 8 (25.00%)	8 / 55 (14.55%)
occurrences (all)	5	3	11
DEHYDRATION			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	1 / 55 (1.82%)
occurrences (all)	0	3	1
ENZYME ABNORMALITY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
HYPERCALCAEMIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 55 (3.64%)
occurrences (all)	0	5	2
HYPERKALAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
HYPERURICAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 55 (5.45%)
occurrences (all)	0	6	3
HYPOALBUMINAEMIA			

subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 55 (1.82%)
occurrences (all)	2	0	2
HYPOCALCAEMIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	5 / 55 (9.09%)
occurrences (all)	1	0	5
HYPOKALAEMIA			
subjects affected / exposed	3 / 9 (33.33%)	3 / 8 (37.50%)	16 / 55 (29.09%)
occurrences (all)	3	6	22
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 9 (22.22%)	1 / 8 (12.50%)	11 / 55 (20.00%)
occurrences (all)	2	6	19
HYPONATRAEMIA			
subjects affected / exposed	1 / 9 (11.11%)	2 / 8 (25.00%)	1 / 55 (1.82%)
occurrences (all)	1	5	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
MALNUTRITION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2: Enrolled at Lenalidomide Dose 25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 34 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
LIPOMA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
TUMOUR PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Vascular disorders			

DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HOT FLUSH			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HYPERTENSION			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	15		
HYPOTENSION			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
PERIPHERAL COLDNESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
VARICOSE VEIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
ADVERSE DRUG REACTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ASTHENIA			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
CHEST DISCOMFORT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CHEST PAIN			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
CHILLS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
FACE OEDEMA			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FATIGUE			
subjects affected / exposed	16 / 34 (47.06%)		
occurrences (all)	22		
GAIT DISTURBANCE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INFUSION SITE SWELLING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INJECTION SITE PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MALAISE			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
NODULE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OEDEMA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OEDEMA PERIPHERAL			
subjects affected / exposed	8 / 34 (23.53%)		
occurrences (all)	10		
PAIN			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PERIPHERAL SWELLING			

subjects affected / exposed occurrences (all)	4 / 34 (11.76%) 4		
PYREXIA subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3		
VESSEL PUNCTURE SITE BRUISE subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
HYPERSENSITIVITY subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2		
HYPOGAMMAGLOBULINAEMIA subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
SEASONAL ALLERGY subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Social circumstances PHYSICAL ASSAULT subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Reproductive system and breast disorders GENITAL RASH subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
OEDEMA GENITAL subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
VAGINAL HAEMORRHAGE subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2		
Respiratory, thoracic and mediastinal disorders			

ALLERGIC SINUSITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
APHONIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
COUGH			
subjects affected / exposed	13 / 34 (38.24%)		
occurrences (all)	19		
DYSPHONIA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
DYSPNOEA			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	9		
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EPISTAXIS			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
HICCUPS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HYPOXIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
LUNG DISORDER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NASAL CONGESTION			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	5		
NASAL DRYNESS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		

NASAL SEPTUM PERFORATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PLEURAL EFFUSION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PNEUMONITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PRODUCTIVE COUGH			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	5		
RESPIRATORY DISORDER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
RHINORRHOEA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
SINUS CONGESTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
UPPER RESPIRATORY TRACT CONGESTION			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
WHEEZING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
YAWNING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
CONFUSIONAL STATE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DEPRESSION			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
DISORIENTATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INSOMNIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
IRRITABILITY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
STRESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	5		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	3		
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
BLOOD CREATINE INCREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BODY TEMPERATURE FLUCTUATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CARDIAC MURMUR			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	12		
LYMPHOCYTE COUNT DECREASED			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	5		
STAPHYLOCOCCUS TEST POSITIVE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
VITAMIN D DECREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
WEIGHT DECREASED			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	8		
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	8		
EYE CONTUSION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FALL			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
IMPACTED FRACTURE			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
LIMB INJURY			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MOUTH INJURY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NAIL INJURY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
POST PROCEDURAL HAEMATOMA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PROCEDURAL PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RIB FRACTURE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SCRATCH			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN ABRASION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN LACERATION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
WOUND			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PALPITATIONS			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
TACHYCARDIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ATAXIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BALANCE DISORDER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DIZZINESS			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	7		
DIZZINESS POSTURAL			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DYSARTHRIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DYSGEUSIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HEAD DISCOMFORT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HEADACHE			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	6		
HYPOAESTHESIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PARAESTHESIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PARKINSON'S DISEASE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PERIPHERAL SENSORIMOTOR NEUROPATHY			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	14		
PRESYNCOPE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		

RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SCIATICA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SPEECH DISORDER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SYNCOPE			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
TREMOR			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	11 / 34 (32.35%)		
occurrences (all)	16		
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	6		
LEUKOCYTOSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
LEUKOPENIA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	6		
LYMPHADENOPATHY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
LYMPHOCYTOSIS			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
LYMPHOPENIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NEUTROPENIA			
subjects affected / exposed	14 / 34 (41.18%)		
occurrences (all)	68		
PANCYTOPENIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
THROMBOCYTOPENIA			
subjects affected / exposed	10 / 34 (29.41%)		
occurrences (all)	36		
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EAR PAIN			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
HYPOACUSIS			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
VERTIGO			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CHALAZION			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DRY AGE-RELATED MACULAR DEGENERATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DRY EYE			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	8		
EXOPHTHALMOS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EYE OEDEMA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EYE PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EYE PRURITUS			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
LACRIMATION INCREASED			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
METAMORPHOPSIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OPTIC NERVE COMPRESSION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PERIORBITAL SWELLING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		

PHOTOPHOBIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
TRICHIASIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
VISION BLURRED			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
VISUAL ACUITY REDUCED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ABDOMINAL PAIN			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	10		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
CONSTIPATION			
subjects affected / exposed	10 / 34 (29.41%)		
occurrences (all)	13		
DEFAECATION URGENCY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DIARRHOEA			

subjects affected / exposed	13 / 34 (38.24%)		
occurrences (all)	29		
DRY MOUTH			
subjects affected / exposed	8 / 34 (23.53%)		
occurrences (all)	8		
DYSPEPSIA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FAECES DISCOLOURED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FLATULENCE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GASTRITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GINGIVAL PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GINGIVAL SWELLING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GLOSSODYNIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		

HAEMATEMESIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HAEMORRHOIDS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HYPERCHLORHYDRIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MELAENA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
MOUTH ULCERATION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
NAUSEA			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	15		
ORAL DISORDER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ORAL PAIN			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
STOMATITIS			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	17		

TONGUE ULCERATION subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
TOOTH LOSS subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
TOOTHACHE subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
VOMITING subjects affected / exposed 5 / 34 (14.71%) occurrences (all) 8			
Hepatobiliary disorders CHOLELITHIASIS subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
HEPATIC CYST subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
HEPATIC FUNCTION ABNORMAL subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
HEPATOMEGALY subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
HYPERBILIRUBINAEMIA subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
Skin and subcutaneous tissue disorders ACNE subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
ACTINIC KERATOSIS subjects affected / exposed 0 / 34 (0.00%) occurrences (all) 0			
BLISTER			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BLOOD BLISTER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DERMATITIS ACNEIFORM			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
DERMATITIS CONTACT			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DRY SKIN			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	7		
ECCHYMOSIS			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
ECZEMA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		
ERYTHEMA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
HYPERHIDROSIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
INGROWING NAIL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MACULE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NIGHT SWEATS			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
ONYCHOCLASIS			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PETECHIAE			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
PRURITUS			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	8		
PURPURA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RASH			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
RASH ERYTHEMATOUS			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	7		
RASH MACULAR			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
RASH MACULO-PAPULAR			
subjects affected / exposed	12 / 34 (35.29%)		
occurrences (all)	35		
RASH PRURITIC			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SCAB			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN DISCOLOURATION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
SKIN EXFOLIATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN FISSURES			

subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
SKIN HYPERPIGMENTATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN IRRITATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SKIN LESION			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
STASIS DERMATITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
BLADDER TRABECULATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
DYSURIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
HAEMATURIA			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
URETHRAL STENOSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
URINARY INCONTINENCE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
URINARY RETENTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	7		
BACK PAIN			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
BONE PAIN			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
FLANK PAIN			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
GROIN PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
JOINT SWELLING			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MUSCLE ATROPHY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MUSCLE SPASMS			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	10		
MUSCLE TIGHTNESS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	6		
MUSCULOSKELETAL DISCOMFORT			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
MYALGIA			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	8		
NECK PAIN			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PAIN IN EXTREMITY			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	8		
PAIN IN JAW			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RHABDOMYOLYSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Infections and infestations			
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BLISTER INFECTED			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
BRONCHITIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		

CHRONIC SINUSITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CLOSTRIDIUM COLITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CONJUNCTIVITIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
CONJUNCTIVITIS BACTERIAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
CORONAVIRUS INFECTION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
CYSTITIS KLEBSIELLA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
EYE INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FOLLICULITIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	3		
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
FURUNCLE			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
GASTROENTERITIS VIRAL			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HERPES ZOSTER			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
IMPETIGO			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
INFLUENZA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
NAIL INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
NASOPHARYNGITIS			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ORAL CANDIDIASIS			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	5		
OTITIS EXTERNA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
OTITIS MEDIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
PHARYNGITIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PNEUMONIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
PSEUDOMONAS INFECTION			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
PUSTULE			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
RASH PUSTULAR			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	5		
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
RHINOVIRUS INFECTION			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
SINUSITIS			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	6		
SINUSITIS BACTERIAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
TINEA PEDIS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	6		
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
WOUND ABSCESS			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
WOUND INFECTION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
WOUND INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	7		
DEHYDRATION			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
ENZYME ABNORMALITY			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HYPERCALCAEMIA			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	5		
HYPERKALAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
HYPERURICAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
HYPOALBUMINAEMIA			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
HYPOCALCAEMIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
HYPOKALAEMIA			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	7		
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
HYPONATRAEMIA			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
MALNUTRITION			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2014	- Updating of safety language for Other Malignancies safety observation. - Study Objectives were updated to provide clarification to the Phase 1 and 2 Primary Objectives, the Phase 2 Secondary Objectives, and the Exploratory Objectives. - Relapsed and refractory disease definitions were clarified. - Ibrutinib and lenalidomide administration was updated to remove dosing restrictions. - Phase 1b Dosing Levels was updated to include cohort information. - Collection of subsequent anti-cancer therapy was updated from all subsequent anticancer therapies to only the first anti-cancer therapy after discontinuation of treatment. - Subject Completion and Withdrawal section was updated to include DLT as a reason for treatment discontinuation.
03 February 2015	- Include the dose re-escalation strategy and rationale to a higher dose level after Dose Level -1 and a dose escalation to 25 mg of lenalidomide since DLBCL is a more aggressive lymphoma (than follicular lymphoma) and may require higher doses. - Clarify the DLT definition in regard to the adverse event of rash and to allow transfusional support during the DLT observation period. - Update the Study Design to allow over-enrollment while keeping the same DLT and cohort expansion criteria in the Phase 1b cohort and update the expected subjects number. - Update the Inclusion and Exclusion Criteria. - Add rash management guidelines. - Add the analysis of serum immunoglobulins as an exploratory objective. - Provide clarity to the lenalidomide prescribing information for US and Ex-US sites per Celgene Corporation's REMS and PPP requirements. - Provide updated reporting requirements on "Other Malignancies" and "Pregnancy". - Update the response criteria for Phase 2 subjects only to reflect the revised criteria being used in the scientific community, updated response criteria were published in 2014 (Cheson et al, 2014).
13 July 2015	- Clarify the DLT definition in regard to TLS, neutropenia, and deep venous thrombosis. - Allow subjects with a DLT to continue study treatment if the treating physician and sponsor expect clinical benefit for the subject. - Modify overdose instructions to align with Pharmacocyclics updated safety language. - Update ibrutinib dose reduction guideline for concomitant use of strong or moderate CYP3A inhibitors.
10 November 2015	- As the use of rituximab in the DLBCL salvage setting is considered standard and to maximize potential efficacy in a patient population with relapsed/refractory and aggressive DLBCL, the Phase 2 study design was amended to remove the randomization and the arm with the 2-drug combination of ibrutinib and lenalidomide without rituximab. - Based on efficacy and safety considerations outlined in the protocol, the dose of 20 mg lenalidomide was proposed as the recommended Phase 2 dose, if determined to be safe and tolerated in Phase 1b. Additional subjects may receive 25 mg lenalidomide as outlined. - Updates per the revised Ibrutinib Investigator's Brochure version 9.0 have been implemented.

01 June 2016	- Included preliminary safety data from the Phase 1b into the protocol to support initiation of the Phase 2 portion of the trial. - Amended that the primary analysis for all efficacy endpoints will be conducted based on the response-evaluable population with de novo non-GCB subtype DLBCL, and not the All-treated population. - Revised based on the updated Imbruvica® label and statistical analysis plan. - Updated to include that a Celgene designee may provide counseling to subjects per Celgene's guidance. - Added Currently active, clinically significant hepatic impairment Child-Pugh class B or C according to the Child-Pugh classification as an exclusion criterion. - Update the use of concomitant medications including that use of QT prolonging agents is no longer restricted. - Updated to specify the number of subjects that will be included for PK collection in the 20 mg and 25 mg lenalidomide cohorts in Phase 2.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported