Clinical trial results:
Phase 3 Study of Ibrutinib in Combination with Venetoclax in Subjects with Mantle Cell Lymphoma

Summary

EudraCT number	2017-000129-12
Trial protocol	GB CZ DE BE HU ES NL GR IT
Global end of trial date	27 June 2024

Results information

Result version number	v1 (current)
This version publication date	27 June 2025
First version publication date	27 June 2025

Trial information

Trial identification

Sponsor protocol code	PCYC-1143-CA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03112174
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	27 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety Run-in: To evaluate the occurrence of TLS and DLTs with the concurrent administration of ibrutinib and venetoclax.
Randomization Phase: To evaluate whether the combination of ibrutinib and venetoclax will result in prolongation of PFS compared to ibrutinib and placebo in subjects with relapsed or refractory MCL.
Treatment-naive Open-label Arm: To evaluate the complete response (CR) rate with the combination of ibrutinib and venetoclax in
subjects with treatment-naive MCL.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Czechia: 38
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Türkiye: 7
Country: Number of subjects enrolled	Ukraine: 15
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	United States: 81

Worldwide total number of subjects	366
EEA total number of subjects	205

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	108
From 65 to 84 years	253
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures were performed up to 28 days before the first dose of ibrutinib and venetoclax/placebo, unless otherwise specified, and may have been performed over more than 1 visit.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Blinding implementation details:

For the Randomization Phase, subjects, investigators, and the Sponsor’s study team members remained blinded to treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Safety Run-in: Increased TLS Risk at Baseline

Arm description:

Participants with an increased risk of tumor lysis syndrome (TLS) enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.

Arm type	Experimental
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Arm title	Safety Run-in: Low TLS Risk at Baseline

Arm description:

Participants with an low risk of TLS enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.

Arm type	Experimental
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details: Administered orally once daily	
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally once daily	
Arm title	Randomization Phase: Ibrutinb + Venetoclax

Arm description:

Participants were randomized to ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg) for approximately 104 weeks, followed by ibrutinib monotherapy until disease progression (PD), unacceptable toxicity or withdrawal of consent. Venetoclax was discontinued after 104 weeks of treatment, regardless of response assessment.

Arm type	Experimental
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally once daily	
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally once daily	
Arm title	Randomization Phase: Ibrutinib + Placebo

Arm description:

Participants were randomized to ibrutinib 560 mg and placebo for approximately 104 weeks, followed by ibrutinib monotherapy until PD, unacceptable toxicity or withdrawal of consent. Placebo was discontinued after 104 weeks of treatment, regardless of response assessment.

Arm type	Placebo
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally once daily	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally once daily	
Arm title	Treatment-naive Open-label Arm

Arm description:	
Participants were treated with ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg).	
Arm type	Experimental
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Administered orally once daily	
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Administered orally once daily	

Number of subjects in period 1	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline	Randomization Phase: Ibrutinb + Venetoclax
Started	15	6	134
On Study Treatment at Study Closure (SC)	0 [1]	2	31 [2]
Off Treatment + On Study Follow Up at SC	2	0 [3]	22 [4]
Already Off Study at Study Closure	13	4	81
Completed	2	2	53
Not completed	13	4	81
Consent withdrawn by subject	3	-	11
Death	8	3	67
Other, not specified	1	-	1
Lost to follow-up	1	1	2

Number of subjects in period 1	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm
Started	133	78
On Study Treatment at Study Closure (SC)	21 [5]	26 [6]
Off Treatment + On Study Follow Up at SC	25 [7]	25 [8]
Already Off Study at Study Closure	87	27 [9]
Completed	46	51
Not completed	87	27
Consent withdrawn by subject	9	7
Death	73	18
Other, not specified	2	-

Lost to follow-up	3	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone data are correct as presented.

Baseline characteristics

Reporting groups	
Reporting group title	Safety Run-in: Increased TLS Risk at Baseline
Reporting group description:	
Participants with an increased risk of tumor lysis syndrome (TLS) enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.	
Reporting group title	Safety Run-in: Low TLS Risk at Baseline
Reporting group description:	
Participants with an low risk of TLS enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.	
Reporting group title	Randomization Phase: Ibrutinb + Venetoclax
Reporting group description:	
Participants were randomized to ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg) for approximately 104 weeks, followed by ibrutinib monotherapy until disease progression (PD), unacceptable toxicity or withdrawal of consent. Venetoclax was discontinued after 104 weeks of treatment, regardless of response assessment.	
Reporting group title	Randomization Phase: Ibrutinib + Placebo
Reporting group description:	
Participants were randomized to ibrutinib 560 mg and placebo for approximately 104 weeks, followed by ibrutinib monotherapy until PD, unacceptable toxicity or withdrawal of consent. Placebo was discontinued after 104 weeks of treatment, regardless of response assessment.	
Reporting group title	Treatment-naive Open-label Arm
Reporting group description:	
Participants were treated with ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg).	

Reporting group values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline	Randomization Phase: Ibrutinb + Venetoclax
Number of subjects	15	6	134
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	2	5	41
>=65 years	13	1	93
Gender categorical Units: Subjects			
Female	6	2	31
Male	9	4	103
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	8
Not Hispanic or Latino	11	5	112
Unknown or Not Reported	3	1	14
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	0	0	1
White	12	6	116
More than one race	0	0	0
Unknown or Not Reported	3	0	15

Reporting group values	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	Total
Number of subjects	133	78	366
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	47	13	108
>=65 years	86	65	258
Gender categorical Units: Subjects			
Female	25	25	89
Male	108	53	277
Ethnicity Units: Subjects			
Hispanic or Latino	7	1	17
Not Hispanic or Latino	110	72	310
Unknown or Not Reported	16	5	39
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	6	11
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	3
White	115	68	317
More than one race	0	0	0
Unknown or Not Reported	14	3	35

End points

End points reporting groups

Reporting group title	Safety Run-in: Increased TLS Risk at Baseline
Reporting group description:	
Participants with an increased risk of tumor lysis syndrome (TLS) enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.	
Reporting group title	Safety Run-in: Low TLS Risk at Baseline
Reporting group description:	
Participants with an low risk of TLS enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.	
Reporting group title	Randomization Phase: Ibrutinb + Venetoclax
Reporting group description:	
Participants were randomized to ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg) for approximately 104 weeks, followed by ibrutinib monotherapy until disease progression (PD), unacceptable toxicity or withdrawal of consent. Venetoclax was discontinued after 104 weeks of treatment, regardless of response assessment.	
Reporting group title	Randomization Phase: Ibrutinib + Placebo
Reporting group description:	
Participants were randomized to ibrutinib 560 mg and placebo for approximately 104 weeks, followed by ibrutinib monotherapy until PD, unacceptable toxicity or withdrawal of consent. Placebo was discontinued after 104 weeks of treatment, regardless of response assessment.	
Reporting group title	Treatment-naive Open-label Arm
Reporting group description:	
Participants were treated with ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg).	

Primary: Number of Participants With Tumor Lysis Syndrome (TLS) Events (Safety Run-in)

End point title	Number of Participants With Tumor Lysis Syndrome (TLS) Events (Safety Run-in)[1][2]
End point description:	
TLS events are defined as follows: • Clinical TLS: any event that meets Howard criteria (N Engl J Med 2011;364:1844-1854) with the following exceptions: • For the purpose of TLS assessment during the Safety Run-in Period, only those increases in serum creatinine > 1.0 mg/dL from pre-treatment baseline will be considered clinical TLS. • In subjects with renal dysfunction at baseline (CrCl < 60 mL/min), clinical TLS is defined as the presence of laboratory TLS plus either seizures, cardiac dysrhythmia, or death. • Laboratory TLS: any event that meets Howard criteria (N Engl J Med 2011;364:1844-1854) for laboratory TLS, that does not resolve within 72 hours despite protocol required management.	
All treated safety run-in participants	
End point type	Primary
End point timeframe:	
After at least 3 months of treatment, with an overall median treatment duration of 20.0 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 per protocol are presented in the data table.

[2] - 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 was specified for the Safety Run-in arm only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	6		
Units: participants	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Dose Limiting Toxicities (DLT) (Safety Run-in)

End point title	Number of Participants With Dose Limiting Toxicities (DLT) (Safety Run-in)[3][4]

End point description:

DLT: any Grade (Gr) 3 or higher non-TLS adverse event (AE) at least possibly related to study drug occurring during the DLT assessment period with the following clarifications:
Non-Hematologic DLTs: Gr ≥3 nausea, vomiting or diarrhea uncontrolled despite maximum medical supportive care and persisting >5 days; Gr 3 fatigue persisting >7 days; Gr 3 infection is not a DLT, however an infection with life-threatening consequences or requiring urgent intervention (Gr 4) was considered a DLT; Treatment delay of any study drug >7 days for toxicity.
Hematologic DLTs: Gr 3 neutropenia is not a DLT, however, Gr 4 neutropenia (ANC <500/mm^3) lasting for > 7 days is a DLT; Gr 3 or 4 neutropenia complicated by fever ≥38.5°C or infection; Gr 4 thrombocytopenia (<25,000/mm^3) that persists for > 7 days; Gr 3 or 4 thrombocytopenia associated with Gr 2 or greater bleeding; Gr 3 anemia is not a DLT, however, Gr 4 anemia is a DLT; Treatment delay of any study drug >7 days for hematologic toxicity.

End point type	Primary

End point timeframe:

After at least 3 months of treatment, with an overall median treatment duration of 20.0 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics per protocol are presented in the data table.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, this endpoint was specified for the Safety Run-in only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	6		
Units: participants				
Any TEAE/Any Grade	3	0		
Any TEAE/ Grade 3+4	3	0		
Any TEAE/Grade 5	0	0		
Atrial fibrillation/Any Grade	1	0		
Atrial fibrillation/Grade 3+4	1	0		
Atrial fibrillation/Grade 5	0	0		
Infection/Any Grade	1	0		
Infection/Grade 3+4	1	0		
Infection/Grade 5	0	0		
Neutropenia/Any Grade	1	0		

Neutropenia/Grade 3+4	1	0		
Neutropenia/Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) (Safety Run-in)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) (Safety Run-in)[5][6]

End point description:

AE: any untoward medical occurrence in a participant that does not necessarily have a causal relationship with treatment. The investigator assesses the relationship of each event to the use of study. Serious adverse event (SAE): an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly,
persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs): any event that began or worsened in severity on or after the first dose of study drug (SD). Event severity is graded as mild (1), moderate (2), severe (3), life threatening (4), death (5).

All treated safety run-in participants

End point type	Primary

End point timeframe:

From first dose of study drug until the end of treatment + 30 days, with an overall median treatment duration of 20.0 months

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics per protocol are presented in the data table.

[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: Per protocol, this endpoint was specified for the Safety Run-in only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	6		
Units: participants				
Any TEAE	15	6		
Any TEAE, Grade 3	15	5		
Any Venetoclax (V) Related TEAE	14	6		
Any V Related TEAE Grade >=3	13	4		
Any Ibrutinib (I) Related TEAE	13	5		
Any I Related TEAE Grade >=3	12	4		
TEAE Leading to Discontinuation of SD (I or V)	6	2		
TEAE Leading to Discontinuation of SD (I only)	1	0		
TEAE Leading to Discontinuation of SD (V only)	1	0		

TEAE Leading to Discontinuation of SD (Both I + V)	4	2		
TEAE Leading to Dose Reduction of SD (I or V)	7	4		
TEAE Leading to Dose Reduction of SD (I only)	1	3		
TEAE Leading to Dose Reduction of SD (V only)	3	0		
TEAE Leading to Dose Reduction of SD (Both I + V)	3	1		
TEAE Leading to Dose Hold of SD (I or V)	14	4		
TEAE Leading to Dose Hold of SD (I Only)	1	1		
TEAE Leading to Dose Hold of SD (V Only)	0	0		
TEAE Leading to Dose Hold of SD (Both I + V)	13	3		
Any TESAE	14	3		
Any TESAE, Grade >=3	14	2		
Any TESAE, V Related	9	1		
Any TESAE, I Related	10	1		
Any TESAE, V or I Related	10	1		
Fatal TEAE	1	0		
Major Hemorrhage	2	0		
Major Hemorrhage, Grade >=3	2	0		
Major Hemorrhage, TESAE	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Progression-free Survival (PFS) (Randomization Phase)

End point title	Progression-free Survival (PFS) (Randomization Phase)[7]

End point description:

PFS is defined as the time from the date of randomization to the date of disease progression using the Revised Response Criteria for Malignant Lymphoma (Cheson 2014), or death from any cause, whichever occurs first.

All randomized participants

End point type	Primary

End point timeframe:

For an overall median time on study of 61.34 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: Per protocol, this endpoint was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	133		
Units: months				
median (confidence interval 95%)	31.9 (22.8 to 54.5)	22.1 (16.5 to 29.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0024 [8]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.629
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.465
upper limit	0.85

Notes:

[8] - P value is from stratified log-rank test.

Primary: Complete Response (CR) Rate (Treatment-Naive Arm)

End point title	Complete Response (CR) Rate (Treatment-Naive Arm)[9][10]

End point description:

CR rate is defined as the percentage of participants with a CR according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2014).

End point type	Primary

End point timeframe:

For an overall median time on study of 40.51 months

Notes:

[9] - 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: Statistical analysis per protocol is presented in the data table.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, this endpoint was specified for the Treatment Naïve Arm only.

End point values	Treatment-naive Open-label Arm			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: percentage of participants				
number (confidence interval 95%)	69.2 (57.8 to 79.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) (Safety Run-in)

End point title	Overall Response Rate (ORR) (Safety Run-in)[11]

End point description:

ORR is defined as the percentage of participants with CR or PR per investigator assessment according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2014).

All enrolled safety run-in participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 74.78 months

Notes:

[11] - 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 was specified for the Safety Run-in only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	6		
Units: percentage of participants				
number (confidence interval 95%)	80.0 (51.9 to 95.7)	83.3 (35.9 to 99.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) (Safety Run-in)

End point title	Duration of Response (DOR) (Safety Run-in)[12]

End point description:

DOR is defined for participants who achieve an overall response as the time from the first occurrence of response (CR or PR according to the Revised Response Criteria for Malignant Lymphoma [Cheson 2014]) to disease progression or death, whichever occurs first.

All enrolled safety run-in participants achieving response (partial response or better)

End point type	Secondary

End point timeframe:

For an overall median time on study of 74.78 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 was specified for the Safety Run-in only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12[13]	5[14]		
Units: months				
median (confidence interval 95%)	44.1 (12.5 to 999999)	999999 (26.5 to 999999)		

Notes:

[13] - 999999=Not estimable due to the small number of events.

[14] - 999999=Not estimable due to the small number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) (Safety Run-in)

End point title	Progression-free Survival (PFS) (Safety Run-in)[15]

End point description:

PFS is defined as the time from the date of the first dose of study treatment to the date of disease progression using the Revised Response Criteria for Malignant Lymphoma (Cheson 2014), or death from any cause, whichever occurs first.

All enrolled safety run-in participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 74.78 months

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: Per protocol, this endpoint was specified for the Safety Run-in arm only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[16]	6[17]		
Units: months				
median (confidence interval 95%)	46.9 (13.0 to 999999)	35.0 (1.2 to 999999)		

Notes:

[16] - 999999=Not estimable due to the small number of events.

[17] - 999999=Not estimable due to the small number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) (Safety Run-in)

End point title	Overall Survival (OS) (Safety Run-in)[18]

End point description:

OS is defined as the time from the date of the first dose of study treatment to death from any cause.

End point type	Secondary

End point timeframe:

For an overall median time on study of 74.78 months

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, this endpoint was specified for the Safety Run-in only.

End point values	Safety Run-in: Increased TLS Risk at Baseline	Safety Run-in: Low TLS Risk at Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[19]	6[20]		
Units: months				
median (confidence interval 95%)	52.3 (14.1 to 999999)	999999 (1.5 to 999999)		

Notes:

[19] - 999999=not estimable due to the small number of events

[20] - 999999=not estimable due to the small number of events

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Complete Response (CR) (Randomization Phase)

End point title	Percentage of Participants With a Complete Response (CR) (Randomization Phase)[21]

End point description:

Complete response rate (CR) based on the best overall response per investigator assessment according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2014).

All randomized participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, this endpoint was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	133		
Units: percentage of particiapnts				
number (confidence interval 95%)	53.7 (44.9 to 62.4)	32.3 (24.5 to 41.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.0004 [23]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Rate Ratio
Point estimate	1.658
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	2.218

Notes:

[22] - For rate ratio, numerator is Ibrutinib + Venetoclax arm and denominator is Ibrutinib + Placebo arm.

[23] - Estimate and p-value for rate ratio are based on Cochran-Mantel-Haenszel (CMH) test adjusted for two randomization stratification factors: number of prior lines of therapy (1-2 vs >=3) and TLS category (low risk vs increased risk) at randomization.

Secondary: Overall Response Rate (ORR) (Randomization Phase and Treatment-Naive Arm)

End point title	Overall Response Rate (ORR) (Randomization Phase and Treatment-Naive Arm)[24]

End point description:

ORR is defined as the percentage of participants with CR or PR per investigator assessment according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2014).

All randomized participants and all treatment-naive open-label arm participants.

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months (Randomization Phase) and 40.51 months (Treatment-Naïve arm)

Notes:

[24] - 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 was specified for the Randomization Phase and the Treatment Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	133	78	
Units: percentage of participants				
number (confidence interval 95%)	82.1 (74.5 to 88.2)	74.4 (66.2 to 81.6)	94.9 (87.4 to 98.6)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

For rate ratio, numerator is Ibrutinib + Venetoclax arm and denominator is Ibrutinib + Placebo arm.

Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1279 [25]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Rate Ratio
Point estimate	1.101
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.973
upper limit	1.247

Notes:

[25] - Estimate and p-value for rate ratio are based on CMH test adjusted for two randomization stratification factors: number of prior lines of therapy (1-2 vs >=3) and TLS category (low risk vs increased risk) at randomization.

Secondary: MRD-negative Remission Rate in Participants Who Achieve CR Per Investigator Assessment (Randomization Phase and Treatment-Naive Arm)

End point title	MRD-negative Remission Rate in Participants Who Achieve CR Per Investigator Assessment (Randomization Phase and Treatment-Naive Arm)[26]

End point description:

MRD-negative remission rate is defined as the percentage of participants with undetectable MRD at documented CR in participants who were MRD positive at screening as assessed by flow cytometry in bone marrow and/or peripheral blood, with requirement of confirmation of MRD negativity in the subsequent peripheral blood 12 weeks later.

All enrolled treatment-naïve participants achieving CR who were evaluable for MRD (those who had positive MRD status at screening). Participants with a given post-screening sample.

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months (Randomization Phase) and 40.51 months (Treatment-Naïve arm)

Notes:

[26] - 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 was specified for the Randomization Phase and the Treatment Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[27]	8[28]	34[29]	
Units: percentage of participants				
number (confidence interval 95%)				
Bone marrow aspirate; n=26, 7, 22	61.5 (40.6 to 79.8)	28.6 (3.7 to 71.0)	59.1 (36.4 to 79.3)	
Peripheral blood; n=31, 8, 34	77.4 (58.9 to 90.4)	12.5 (0.3 to 52.7)	76.5 (58.8 to 89.3)	

Notes:

[27] - n=participants with an assessment

[28] - n=participants with an assessment

[29] - n=participants with an assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Bone marrow aspirate	
Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2028
Method	Fisher exact

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Peripheral blood	
Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014
Method	Fisher exact

Secondary: Overall Survival (OS) (Randomization Phase and Treatment-Naive Arm)	
End point title	Overall Survival (OS) (Randomization Phase and Treatment-Naive Arm)[30]

End point description:

OS is defined as the time from the date of randomization (Randomization Phase) or the first dose of study treatment (Treatment-Naïve arm) to death from any cause.

All randomized and all enrolled treatment-naïve participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months (Randomization Phase) and 40.51 months (Treatment-Naïve arm)

Notes:

[30] - 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 was specified for the Randomization Phase and Treatment-Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134[31]	133	78[32]	
Units: months				
median (confidence interval 95%)	44.9 (31.9 to 999999)	38.6 (25.2 to 52.6)	999999 (44.2 to 999999)	

Notes:

[31] - 999999=not estimable due to small number of events.

[32] - 999999=not estimable due to the small number of events.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Hazard ratio is estimated using stratified Cox regression model with treatment as the only covariate.	
Comparison groups	Randomization Phase: Ibrutinib + Placebo v Randomization Phase: Ibrutinb + Venetoclax
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2669 [33]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.832
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.602
upper limit	1.151

Notes:

[33] - P value is from stratified log-rank test.

Secondary: Duration of Response (DOR) (Randomization Phase and Treatment-Naive Arm)

End point title	Duration of Response (DOR) (Randomization Phase and Treatment-Naive Arm)[34]

End point description:

DOR is defined as the time frame for participants who achieve an overall response as the time from the first occurrence of response (CR or PR according to the Revised Response Criteria for Malignant Lymphoma [Cheson 2014]) to disease progression or death, whichever occurs first.

All randomized participants and all enrolled treatment-naïve participants achieving response (partial response or better)

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months (Randomization Phase) and 40.51 months (Treatment-Naïve arm)

Notes:

[34] - 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 was specified for the Randomization Phase and Treatment-Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110[35]	99	74[36]	
Units: months				
median (confidence interval 95%)	42.1 (42.1 to 999999)	27.6 (19.4 to 39.5)	37.1 (30.3 to 999999)	

Notes:

[35] - 999999=Not estimable due to the small number of events.

[36] - 999999=Not estimable due to the small number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Treatment (TTNT) (Randomization Phase and Treatment-Naive Arm)

End point title	Time to Next Treatment (TTNT) (Randomization Phase and Treatment-Naive Arm)[37]

End point description:

TTNT is defined as the duration from the date of randomization (Randomization Phase) or date of first dose of study treatment (Treatment-Naive Arm) to the start date of any anti-lymphoma treatment subsequent to study treatment. Post-treatment stem cell transplantation, chimeric antigen receptor (CAR) T-cell therapy, or other cellular therapies were not considered subsequent anti-cancer treatments for participants responding to the study treatment (CR or PR).

All randomized and all enrolled treatment-naïve participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months (Randomization Phase) and 40.51 months (Treatment-Naïve arm)

Notes:

[37] - 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 was specified for the Randomization Phase and Treatment-Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo	Treatment-naive Open-label Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134[38]	133	74[39]	
Units: months				
median (confidence interval 95%)	999999 (48.0 to 999999)	35.4 (24.7 to 49.8)	999999 (999999 to 999999)	

Notes:

[38] - 999999=Not estimable due to the small number of events.

[39] - 999999=Not estimable due to the small number of events.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Hazard ratio is estimated using stratified Cox regression model with treatment as the only covariate.	
Comparison groups	Randomization Phase: Ibrutinib + Placebo v Randomization Phase: Ibrutinb + Venetoclax
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013 [40]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.541
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.369
upper limit	0.792

Notes:

[40] - P value is from stratified log-rank test.

Secondary: Number of Participants With TEAEs (Randomization Phase)

End point title	Number of Participants With TEAEs (Randomization Phase)[41]

End point description:

AE: any untoward medical occurrence in a participant that does not necessarily have a causal relationship with treatment. The investigator assesses the relationship of each event to the use of study. Serious adverse event (SAE): an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs): any event that began or worsened in severity on or after the first dose of study drug (SD). Event severity is graded as mild (1), moderate (2), severe (3), life threatening (4), death (5).

All randomized and treated participants

End point type	Secondary

End point timeframe:

From first dose of study drug until the end of treatment + 30 days, with an overall median treatment duration of 19.5 months

Notes:

[41] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	132		
Units: participants				
Any TEAE	134	131		
Any TEAE, Grade 3	113	100		
Any Venetoclax (V) Related TEAE	112	104		
Any V Related TEAE Grade >=3	75	46		
Any Ibrutinib (I) Related TEAE	121	114		
Any I Related TEAE Grade >=3	83	58		
TEAE Leading to Discontinuation of SD (I or V)	43	48		
TEAE Leading to Discontinuation of SD (I only)	15	11		
TEAE Leading to Discontinuation of SD (V only)	2	7		
TEAE Leading to Discontinuation of SD (Both I + V)	26	30		
TEAE Leading to Dose Reduction of SD (I or V)	50	29		
TEAE Leading to Dose Reduction of SD (I only)	19	14		
TEAE Leading to Dose Reduction of SD (V only)	13	7		
TEAE Leading to Dose Reduction of SD (Both I + V)	18	8		
TEAE Leading to Dose Hold of SD (I or V)	106	99		
TEAE Leading to Dose Hold of SD (I only)	18	18		
TEAE Leading to Dose Hold of Study Drug (V only)	6	4		
TEAE Leading to Dose Hold of SD (Both I + V)	82	77		
Any TESAE	88	80		
Any TESAE, Grade >=3	76	73		
Any TESAE, V Related	31	25		
Any TESAE, I Related	47	37		
Any TESAE, V or I Related	49	37		
Fatal TEAE	22	18		
Major Hemorrhage	13	8		
Major Hemorrhage, Grade >=3	10	7		
Major Hemorrhage, TESAE	12	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TLS TEAEs (Randomization Phase)

End point title	Number of Participants With TLS TEAEs (Randomization

End point description:

Treatment-emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs): any event that began or worsened in severity on or after the first dose of study drug (SD). Event severity is graded as mild (1), moderate (2), severe (3), life threatening (4), death (5).

All randomized and treated participants

End point type	Secondary

End point timeframe:

From first dose of study drug until the end of treatment + 30 days, with an overall median treatment duration of 19.5 months

Notes:

[42] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	132		
Units: participants				
Any grade	7	3		
Grades 3 and 4	6	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of Ibrutinib: Maximum Observed Plasma Concentration (Cmax) (Randomization Phase)

End point title	Pharmacokinetics (PK) of Ibrutinib: Maximum Observed Plasma Concentration (Cmax) (Randomization Phase)[43]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[43] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	108		
Units: ng/mL				
arithmetic mean (standard deviation)	195 (± 179)	287 (± 230)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Time to Cmax (Tmax) (Randomization Phase)

End point title	PK of Ibrutinib: Time to Cmax (Tmax) (Randomization

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[44] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	108		
Units: hours				
median (full range (min-max))	2.00 (0.00 to 8.00)	2.00 (0.750 to 6.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Area Under the Concentration-Time Curve From Time Zero to the Time of the Last Measurable Concentration (AUClast) (Randomization Phase)

End point title	PK of Ibrutinib: Area Under the Concentration-Time Curve From Time Zero to the Time of the Last Measurable Concentration (AUClast) (Randomization Phase)[45]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[45] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	106		
Units: ng·h/mL				
arithmetic mean (standard deviation)	1090 (± 870)	1440 (± 1060)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Terminal Elimination Half-Life (t1/2,Term) (Randomization Phase)

End point title	PK of Ibrutinib: Terminal Elimination Half-Life (t1/2,Term) (Randomization Phase)[46]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[46] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	73		
Units: hours				
arithmetic mean (standard deviation)	6.29 (± 1.92)	6.66 (± 2.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Time of Last Measurable Concentration (Tlast) (Randomization Phase)

End point title	PK of Ibrutinib: Time of Last Measurable Concentration (Tlast) (Randomization Phase)[47]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[47] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	106		
Units: hours				
median (full range (min-max))	24.0 (7.0 to 24.0)	24.0 (24.0 to 24.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Area Under the Concentration-Time Curve From 0-24 Hours (AUC0-24) (Randomization Phase)

End point title	PK of Ibrutinib: Area Under the Concentration-Time Curve From 0-24 Hours (AUC0-24) (Randomization Phase)[48]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[48] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	106		
Units: ng·h/mL				
arithmetic mean (standard deviation)	1090 (± 870)	1440 (± 1060)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Terminal Elimination Rate Constant (λz) (Randomization Phase)

End point title	PK of Ibrutinib: Terminal Elimination Rate Constant (λz) (Randomization Phase)[49]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[49] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	73		
Units: 1/hour				
arithmetic mean (standard deviation)	0.123 (± 0.0556)	0.114 (± 0.0332)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Ibrutinib: Apparent Total Clearance at Steady State (CLss/F) (Randomization Phase)

End point title	PK of Ibrutinib: Apparent Total Clearance at Steady State (CLss/F) (Randomization Phase)[50]

End point description:

Participants with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[50] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	106		
Units: L/hour				
arithmetic mean (standard deviation)	1020 (± 1130)	709 (± 651)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Venetoclax: Cmax (Randomization Phase)

End point title	PK of Venetoclax: Cmax (Randomization Phase)[51]

End point description:

Participants receiving venetoclax with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[51] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: ng/mL				
arithmetic mean (standard deviation)	3620 (± 1650)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Venetoclax: AUC0-24 (Randomization Phase)

End point title	PK of Venetoclax: AUC0-24 (Randomization Phase)[52]

End point description:

Participants receiving venetoclax with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[52] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: ng·h/mL				
arithmetic mean (standard deviation)	65000 (± 32900)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Venetoclax: Time to Cmax (Tmax) (Randomization Phase)

End point title	PK of Venetoclax: Time to Cmax (Tmax) (Randomization Phase)[53]

End point description:

Participants receiving venetoclax with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[53] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: hours				
median (full range (min-max))	6.00 (0.00 to 8.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Venetoclax: CLss/F (Randomization Phase)

End point title	PK of Venetoclax: CLss/F (Randomization Phase)[54]

End point description:

Participants receiving venetoclax with an evaluable PK assessment at given time point.

End point type	Secondary

End point timeframe:

Week 6, Day 1: Predose, at Dose, 1 hour (± 15 minutes [min]), 2 hours (± 15 min), 4 hours (± 30 min), 6 hours (± 30 min), 8 hours (± 1 hour) post-dose

Notes:

[54] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: L/hour				
geometric mean (standard deviation)	8.09 (± 4.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Worsening in Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) Subscale of the Health-Related Quality of Life (Randomization Phase)

End point title	Time to Worsening in Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) Subscale of the Health-Related Quality of Life (Randomization Phase)[55]

End point description:

The FACT-Lym lymphoma-specific additional concerns subscale responses to all items are rated on a 5-point scale ranging from 0 “not at all” to 4 “very much”. The lymphoma subscale includes 15 items and scores range from 0 to 60, with higher scores representing better functional status and well-being. Worsening is defined by a >=5 points reduction from baseline in FACT-Lym Subscale or death due to any cause, whichever occurs first.

All randomized participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 61.34 months

Notes:

[55] - 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 was specified for the Randomization Phase only.

End point values	Randomization Phase: Ibrutinb + Venetoclax	Randomization Phase: Ibrutinib + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	133		
Units: months				
median (confidence interval 95%)	9.3 (6.5 to 12.7)	12.5 (8.3 to 17.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Hazard ratio is estimated using stratified Cox regression model with treatment as the only covariate.

Comparison groups	Randomization Phase: Ibrutinb + Venetoclax v Randomization Phase: Ibrutinib + Placebo
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2861 [56]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.169
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.879
upper limit	1.554

Notes:

[56] - P value is from stratified log-rank test.

Secondary: Duration of CR (Treatment-Naive Arm)

End point title	Duration of CR (Treatment-Naive Arm)[57]

End point description:

Duration of CR, defined for subjects who achieve CR according to the Revised Response Criteria for Malignant Lymphoma (Cheson 2014) as the time from the first occurrence of CR to disease progression or death, whichever occurs first.

All Enrolled Treatment-Naïve Subjects Achieving Response (Partial Response or Better)

End point type	Secondary

End point timeframe:

For an overall median time on study of 40.51 months

Notes:

[57] - 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 was specified for the Treatment Naïve Arm only.

End point values	Treatment-naive Open-label Arm			
Subject group type	Reporting group			
Number of subjects analysed	74[58]			
Units: months				
median (confidence interval 95%)	37.1 (34.0 to 999999)			

Notes:

[58] - 999999=Not estimable due to the small number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) (Treatment-Naive Arm)

End point title	Progression-free Survival (PFS) (Treatment-Naive Arm)[59]

End point description:

PFS is defined as the time from the date of the first dose of study treatment to the date of disease progression using the Revised Response Criteria for Malignant Lymphoma (Cheson 2014), or death from any cause, whichever occurs first.

All enrolled treatment-naïve participants

End point type	Secondary

End point timeframe:

For an overall median time on study of 40.51 months

Notes:

[59] - 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 was specified for the Treatment Naïve Arm only.

End point values	Randomization Phase: Ibrutinb + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	78[60]			
Units: months				
median (full range (min-max))	40.2 (29.4 to 999999)			

Notes:

[60] - 999999=not estimable due to the low number of events.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

For an overall median duration of 69.6 months (Safety Run-in: Increased TLS Risk), 77.9 months (Safety Run-in: Low TLS Risk), 61.0 months (Randomization Phase: Ibrutinb + Venetoclax), 61.7 months (Randomization Phase: Ibrutinb + Placebo), 40.5 months (Tre

Adverse event reporting additional description:

All treated participants

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Safety Run-in: Low TLS Risk at Baseline

Reporting group description:

Participants with an low risk of TLS enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.

Reporting group title	Safety Run-in: Increased TLS Risk at Baseline

Reporting group description:

Participants with an increased risk of TLS enrolled into the open-label Safety Run-in Period received concurrent ibrutinib at 560 mg once daily and venetoclax starting at 20 mg, and gradually ramped up to a target dose of 400 mg once daily over a 5-week period.

Reporting group title	Treatment-naive Open-label Arm

Reporting group description:

Participants were treated with ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg).

Reporting group title	Randomization Phase: Ibrutinib + Placebo

Reporting group description:

Participants were randomized to ibrutinib 560 mg and placebo for approximately 104 weeks, followed by ibrutinib monotherapy until PD, unacceptable toxicity or withdrawal of consent. Placebo was discontinued after 104 weeks of treatment, regardless of response assessment.

Reporting group title	Randomization Phase: Ibrutinb + Venetoclax

Reporting group description:

Participants were randomized to ibrutinib 560 mg and venetoclax (starting at 20 mg, and gradually ramped up to a target dose of 400 mg) for approximately 104 weeks, followed by ibrutinib monotherapy until disease progression (PD), unacceptable toxicity or withdrawal of consent. Venetoclax was discontinued after 104 weeks of treatment, regardless of response assessment.

Serious adverse events	Safety Run-in: Low TLS Risk at Baseline	Safety Run-in: Increased TLS Risk at Baseline	Treatment-naive Open-label Arm
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	15 / 15 (100.00%)	48 / 78 (61.54%)
number of deaths (all causes)	3	8	20
number of deaths resulting from adverse events	1	1	10
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MANTLE CELL LYMPHOMA RECURRENT			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MANTLE CELL LYMPHOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
LYMPHOMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 ADENOCARCINOMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN LUNG NEOPLASM			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADRENAL NEOPLASM			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTATIC MALIGNANT MELANOMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THYROID CANCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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-SMALL CELL LUNG CANCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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			
AORTIC ANEURYSM			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC STENOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTENSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
ILIAC ARTERY STENOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC DEATH			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PYREXIA			
subjects affected / exposed	0 / 6 (0.00%)	3 / 15 (20.00%)	3 / 78 (3.85%)
occurrences causally related to treatment / all	0 / 0	1 / 3	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GAIT DISTURBANCE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALAISE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEROSITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
GRAFT VERSUS HOST DISEASE IN GASTROINTESTINAL TRACT			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COUGH			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY HYPERTENSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 AIRWAY OBSTRUCTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOCAL CORD POLYP			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPLETED SUICIDE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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			
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPHIL COUNT DECREASED			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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 CREATININE INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
SKULL FRACTURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
FEMUR FRACTURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACCIDENTAL OVERDOSE			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPLENIC RUPTURE			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences causally related to treatment / all	0 / 0	2 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIOSCLEROSIS CORONARY ARTERY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ATRIAL FLUTTER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIAC FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MITRAL VALVE DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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			
AMNESIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYKINESIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
HAEMORRHAGIC STROKE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL HAEMATOMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TREMOR			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPEECH DISORDER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRAVENTRICULAR HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE BONE MARROW APLASIA			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
SPONTANEOUS HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UVEITIS			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATEMESIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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 ISCHAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
NAUSEA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROCTITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETROPERITONEAL HAEMORRHAGE			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
STOMATITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBILEUS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UMBILICAL HERNIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMATOSIS INTESTINALIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STONE			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY COLIC			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 ACUTE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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			
CUTANEOUS VASCULITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECCHYMOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URTICARIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATURIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
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			
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ARTHRALGIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POLYARTHRITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECK PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS LIMB			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL NERVOUS SYSTEM			

INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL SEPSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM COLITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	8 / 78 (10.26%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	6 / 78 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISSEMINATED CRYPTOCOCCOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FUNGAL ABSCESS CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
GASTROENTERITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 INFECTION			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDIASTINITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORCHITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 CHLAMYDIAL			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	5 / 78 (6.41%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 BACTERIAL			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIORBITAL CELLULITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 MORAXELLA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 STREPTOCOCCAL			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY SEPSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (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
WOUND SEPSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
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			
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCALCAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GOUT			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERKALAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LACTIC ACIDOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERURICAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Randomization Phase: Ibrutinib + Placebo	Randomization Phase: Ibrutinb + Venetoclax	
Total subjects affected by serious adverse events			
subjects affected / exposed	86 / 132 (65.15%)	92 / 134 (68.66%)	
number of deaths (all causes)	78	70	
number of deaths resulting from adverse events	29	34	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MANTLE CELL LYMPHOMA RECURRENT			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MANTLE CELL LYMPHOMA			
subjects affected / exposed	18 / 132 (13.64%)	15 / 134 (11.19%)	
occurrences causally related to treatment / all	0 / 27	0 / 23	
deaths causally related to treatment / all	0 / 14	0 / 12	
LYMPHOMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BREAST CANCER			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BENIGN LUNG NEOPLASM			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADRENAL NEOPLASM			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADENOCARCINOMA OF COLON			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
METASTATIC MALIGNANT MELANOMA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
THYROID CANCER			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROSTATE CANCER			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-SMALL CELL LUNG CANCER			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
AORTIC ANEURYSM			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
AORTIC STENOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SHOCK HAEMORRHAGIC			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	3 / 132 (2.27%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILIAC ARTERY STENOSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ISCHAEMIA			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMBOLISM			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC DEATH			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CHEST PAIN			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
PYREXIA			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GAIT DISTURBANCE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			

subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALAISE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEROSITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
GRAFT VERSUS HOST DISEASE IN GASTROINTESTINAL TRACT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			

subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COUGH			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			

subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY HYPERTENSION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY OEDEMA			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	6 / 132 (4.55%)	3 / 134 (2.24%)	
occurrences causally related to treatment / all	2 / 6	2 / 6	
deaths causally related to treatment / all	0 / 2	1 / 2	
UPPER AIRWAY OBSTRUCTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOCAL CORD POLYP			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	4 / 132 (3.03%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPLETED SUICIDE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUICIDAL IDEATION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPHIL COUNT DECREASED			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
SKULL FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIP FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACCIDENTAL OVERDOSE			
subjects affected / exposed	2 / 132 (1.52%)	7 / 134 (5.22%)	
occurrences causally related to treatment / all	2 / 3	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPLENIC RUPTURE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	3 / 132 (2.27%)	6 / 134 (4.48%)	
occurrences causally related to treatment / all	4 / 4	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTERIOSCLEROSIS CORONARY ARTERY			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ATRIAL FLUTTER			
subjects affected / exposed	0 / 132 (0.00%)	5 / 134 (3.73%)	
occurrences causally related to treatment / all	0 / 0	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
CARDIAC FAILURE			
subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	2 / 3	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	3 / 132 (2.27%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			

subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDITIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MITRAL VALVE DISEASE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR FIBRILLATION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
AMNESIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRADYKINESIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGIC STROKE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
EPILEPSY			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
CEREBRAL HAEMATOMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TREMOR			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPEECH DISORDER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRAVENTRICULAR HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 132 (1.52%)	6 / 134 (4.48%)	
occurrences causally related to treatment / all	1 / 2	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE BONE MARROW APLASIA			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	3 / 132 (2.27%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHADENOPATHY			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 132 (3.03%)	4 / 134 (2.99%)	
occurrences causally related to treatment / all	0 / 4	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPONTANEOUS HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
UVEITIS			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATEMESIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOLITIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 132 (0.76%)	3 / 134 (2.24%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGUINAL HERNIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCTITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETROPERITONEAL HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBILEUS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UMBILICAL HERNIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMATOSIS INTESTINALIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
BILE DUCT STONE			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILIARY COLIC			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLANGITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 132 (0.00%)	3 / 134 (2.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLELITHIASIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
CUTANEOUS VASCULITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ECCHYMOSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH MACULO-PAPULAR			

subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URTICARIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
RENAL FAILURE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATURIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 132 (2.27%)	3 / 134 (2.24%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ARTHRALGIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POLYARTHRITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NECK PAIN			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS LIMB			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS PERFORATED			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS BACTERIAL			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CENTRAL NERVOUS SYSTEM			

INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERIAL SEPSIS			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM COLITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19			

subjects affected / exposed	1 / 132 (0.76%)	6 / 134 (4.48%)	
occurrences causally related to treatment / all	0 / 1	2 / 10	
deaths causally related to treatment / all	0 / 0	1 / 4	
COVID-19 PNEUMONIA			
subjects affected / exposed	2 / 132 (1.52%)	5 / 134 (3.73%)	
occurrences causally related to treatment / all	2 / 4	0 / 7	
deaths causally related to treatment / all	1 / 2	0 / 2	
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED CRYPTOCOCCOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FUNGAL ABSCESS CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL INFECTION			

subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMPYEMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MEDIASTINITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NECROTISING FASCIITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ORCHITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOMYELITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA CHLAMYDIAL			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	15 / 132 (11.36%)	17 / 134 (12.69%)	
occurrences causally related to treatment / all	6 / 17	13 / 26	
deaths causally related to treatment / all	0 / 0	0 / 1	
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIORBITAL CELLULITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA MORAXELLA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA STREPTOCOCCAL			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA VIRAL			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY SEPSIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	5 / 132 (3.79%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	2 / 6	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL BACTERAEMIA			

subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 132 (3.03%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND SEPSIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL PHARYNGITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GOUT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERKALAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METABOLIC ACIDOSIS			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
LACTIC ACIDOSIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERURICAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	2 / 132 (1.52%)	4 / 134 (2.99%)	
occurrences causally related to treatment / all	1 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Safety Run-in: Low TLS Risk at Baseline	Safety Run-in: Increased TLS Risk at Baseline	Treatment-naive Open-label Arm
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	15 / 15 (100.00%)	77 / 78 (98.72%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	0	1	3
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
HAEMATOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HYPERTENSION			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	15 / 78 (19.23%)
occurrences (all)	5	4	23
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
ADVERSE DRUG REACTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ASTHENIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	6 / 78 (7.69%)
occurrences (all)	0	3	12
CATHETER SITE BRUISE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
CHILLS			

subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	4 / 78 (5.13%)
occurrences (all)	2	2	6
FATIGUE			
subjects affected / exposed	4 / 6 (66.67%)	5 / 15 (33.33%)	30 / 78 (38.46%)
occurrences (all)	12	12	78
GENERALISED OEDEMA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
IMPAIRED HEALING			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	1	4
INJECTION SITE BRUISING			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
OEDEMA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 6 (50.00%)	2 / 15 (13.33%)	14 / 78 (17.95%)
occurrences (all)	4	2	15
PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	6 / 78 (7.69%)
occurrences (all)	0	1	6
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	1	1	9
PYREXIA			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	16 / 78 (20.51%)
occurrences (all)	1	1	20
SYSTEMIC INFLAMMATORY			

RESPONSE SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
EXTRAVASATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ALLERGY TO ARTHROPOD BITE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	3	2
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
COUGH			
subjects affected / exposed	2 / 6 (33.33%)	5 / 15 (33.33%)	13 / 78 (16.67%)
occurrences (all)	2	5	17
DYSPHONIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	2 / 78 (2.56%)
occurrences (all)	0	2	2
PLEURITIC PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	1	1	3
NASAL DRYNESS			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
NASAL CONGESTION			
subjects affected / exposed	2 / 6 (33.33%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	2	1	5
EPISTAXIS			
subjects affected / exposed	2 / 6 (33.33%)	1 / 15 (6.67%)	6 / 78 (7.69%)
occurrences (all)	7	1	6
DYSPNOEA			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	14 / 78 (17.95%)
occurrences (all)	3	4	23
PULMONARY OEDEMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
SINUS CONGESTION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
SINUS DISORDER			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
VOCAL CORD POLYP			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
WHEEZING			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	4 / 78 (5.13%)
occurrences (all)	1	2	5

CONFUSIONAL STATE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
INSOMNIA			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	9 / 78 (11.54%)
occurrences (all)	2	0	10
DISORIENTATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
DEPRESSION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	3	2	9
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	5 / 78 (6.41%)
occurrences (all)	3	3	11
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	3	0	3
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 6 (33.33%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	6	2	19
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 6 (33.33%)	3 / 15 (20.00%)	7 / 78 (8.97%)
occurrences (all)	3	6	9
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	1	2	0
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0

BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	0	0	2
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	0	1	3
WEIGHT DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	6 / 78 (7.69%)
occurrences (all)	0	4	7
TROPONIN T INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	6 / 78 (7.69%)
occurrences (all)	0	2	10
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	10 / 78 (12.82%)
occurrences (all)	0	2	32
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	6 / 78 (7.69%)
occurrences (all)	3	2	7
FALL			
subjects affected / exposed	1 / 6 (16.67%)	4 / 15 (26.67%)	6 / 78 (7.69%)
occurrences (all)	1	6	9
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
LIMB INJURY			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	1 / 78 (1.28%)
occurrences (all)	0	2	1
SCRATCH			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
SKIN ABRASION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	1	0	5
SKIN LACERATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
THERMAL BURN			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	2	0	0
TRAUMATIC HAEMATOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	10 / 78 (12.82%)
occurrences (all)	0	1	10
BRADYCARDIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
PALPITATIONS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	7 / 78 (8.97%)
occurrences (all)	0	0	10
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 6 (50.00%)	1 / 15 (6.67%)	15 / 78 (19.23%)
occurrences (all)	4	1	21
DYSKINESIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
DYSGEUSIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	4 / 78 (5.13%)
occurrences (all)	0	0	4
DYSARTHRIA			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
DIZZINESS			
subjects affected / exposed	3 / 6 (50.00%)	2 / 15 (13.33%)	17 / 78 (21.79%)
occurrences (all)	21	2	23
PARESIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HYPOAESTHESIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	7 / 78 (8.97%)
occurrences (all)	4	0	19
MEMORY IMPAIRMENT			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	2 / 78 (2.56%)
occurrences (all)	1	3	2
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
PARAESTHESIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	9 / 78 (11.54%)
occurrences (all)	3	0	19
VASCULAR ENCEPHALOPATHY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
TREMOR			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	2 / 78 (2.56%)
occurrences (all)	0	3	2
SYNCOPE			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
SENSORY DISTURBANCE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
RESTLESS LEGS SYNDROME			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
PRESYNCOPE			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	1	2	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	6 / 78 (7.69%)
occurrences (all)	1	0	8
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 6 (33.33%)	4 / 15 (26.67%)	17 / 78 (21.79%)
occurrences (all)	2	20	27
LEUKOPENIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
LYMPHADENOPATHY			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	1	0	2
NEUTROPENIA			
subjects affected / exposed	1 / 6 (16.67%)	7 / 15 (46.67%)	26 / 78 (33.33%)
occurrences (all)	2	33	67
SPLENOMEGALY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	2
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 6 (66.67%)	4 / 15 (26.67%)	8 / 78 (10.26%)
occurrences (all)	5	6	23
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	3 / 6 (50.00%)	3 / 15 (20.00%)	17 / 78 (21.79%)
occurrences (all)	4	4	25
Ear and labyrinth disorders			
EAR PAIN			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
TINNITUS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
VERTIGO			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	3 / 78 (3.85%)
occurrences (all)	1	0	5
Eye disorders			
ASTIGMATISM			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
CATARACT			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	3 / 78 (3.85%)
occurrences (all)	0	2	5
VISUAL ACUITY REDUCED			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	9 / 78 (11.54%)
occurrences (all)	1	3	13
DIPLOPIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	1	0	2
DRY EYE			
subjects affected / exposed	2 / 6 (33.33%)	4 / 15 (26.67%)	8 / 78 (10.26%)
occurrences (all)	3	4	14
EYE DISCHARGE			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	1	1	2
EYE IRRITATION			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	6 / 78 (7.69%)
occurrences (all)	2	5	6
EYE PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
HYPERMETROPIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0

LACRIMATION INCREASED			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	9 / 78 (11.54%)
occurrences (all)	6	2	15
MACULAR DEGENERATION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
MACULOPATHY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
PHOTOPHOBIA			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	3 / 78 (3.85%)
occurrences (all)	3	3	4
PHOTOPSIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	1 / 78 (1.28%)
occurrences (all)	0	2	1
VISION BLURRED			
subjects affected / exposed	3 / 6 (50.00%)	4 / 15 (26.67%)	8 / 78 (10.26%)
occurrences (all)	10	5	17
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
VITREOUS FLOATERS			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	5 / 78 (6.41%)
occurrences (all)	3	2	6
Gastrointestinal disorders			
FLATULENCE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
ABDOMINAL PAIN			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	11 / 78 (14.10%)
occurrences (all)	1	4	20
ABDOMINAL PAIN UPPER			

subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	7 / 78 (8.97%)
occurrences (all)	1	2	8
ANAL HAEMORRHAGE			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
APHTHOUS ULCER			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	5 / 78 (6.41%)
occurrences (all)	1	0	10
CHRONIC GASTRITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
CONSTIPATION			
subjects affected / exposed	2 / 6 (33.33%)	3 / 15 (20.00%)	13 / 78 (16.67%)
occurrences (all)	5	3	19
DIARRHOEA			
subjects affected / exposed	5 / 6 (83.33%)	10 / 15 (66.67%)	37 / 78 (47.44%)
occurrences (all)	21	24	196
DRY MOUTH			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	3 / 78 (3.85%)
occurrences (all)	1	2	4
DUODENITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
DYSPEPSIA			
subjects affected / exposed	3 / 6 (50.00%)	1 / 15 (6.67%)	8 / 78 (10.26%)
occurrences (all)	3	1	12
DYSPHAGIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
ENTERITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
FAECES SOFT			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
FEMORAL HERNIA			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	1	4
GASTRITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	3 / 78 (3.85%)
occurrences (all)	0	0	3
GLOSSODYNIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	4 / 78 (5.13%)
occurrences (all)	0	2	4
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	2	0
MOUTH ULCERATION			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	7 / 78 (8.97%)
occurrences (all)	3	0	13
NAUSEA			
subjects affected / exposed	5 / 6 (83.33%)	5 / 15 (33.33%)	24 / 78 (30.77%)
occurrences (all)	16	15	75
OESOPHAGITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
PEPTIC ULCER			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	12 / 78 (15.38%)
occurrences (all)	3	2	31
TONGUE ERYTHEMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
TONGUE HAEMORRHAGE			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
TOOTHACHE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	5 / 78 (6.41%)
occurrences (all)	0	0	5
VOMITING			
subjects affected / exposed	1 / 6 (16.67%)	5 / 15 (33.33%)	18 / 78 (23.08%)
occurrences (all)	11	9	35
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	11 / 78 (14.10%)
occurrences (all)	0	2	12
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	6 / 78 (7.69%)
occurrences (all)	0	0	8
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	7	2	0
HEPATITIS CHOLESTATIC			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
PORTAL FIBROSIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
ONYCHOCLASIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
PETECHIAE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	7 / 78 (8.97%)
occurrences (all)	0	0	11
ALOPECIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	1	4
BLOOD BLISTER			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	4 / 78 (5.13%)
occurrences (all)	0	0	5
DECUBITUS ULCER			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	2	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	3	0	0
DRY SKIN			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	1	1	4
ECCHYMOSIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
ERYTHEMA			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	2	1	3
HYPERHIDROSIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
NIGHT SWEATS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	1	0	2
PRURITUS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	11 / 78 (14.10%)
occurrences (all)	1	0	13
RASH			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	1	1	2
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	5 / 78 (6.41%)
occurrences (all)	0	1	5
RASH MACULO-PAPULAR			
subjects affected / exposed	2 / 6 (33.33%)	4 / 15 (26.67%)	13 / 78 (16.67%)
occurrences (all)	6	5	19
SKIN LESION			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	0	1	4
URTICARIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	4 / 78 (5.13%)
occurrences (all)	0	0	4
SKIN ULCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	5 / 78 (6.41%)
occurrences (all)	0	0	12
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	6 / 78 (7.69%)
occurrences (all)	0	0	8
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
BLADDER HYPERTROPHY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HAEMATURIA			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	11 / 78 (14.10%)
occurrences (all)	1	2	13
POLLAKIURIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
RENAL FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
URINARY RETENTION			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	2 / 78 (2.56%)
occurrences (all)	0	2	2

NEPHROLITHIASIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	3 / 78 (3.85%)
occurrences (all)	2	0	3
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	8 / 78 (10.26%)
occurrences (all)	1	2	14
OSTEOARTHRITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
NECK PAIN			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
MYALGIA			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	16 / 78 (20.51%)
occurrences (all)	13	3	34
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	3 / 78 (3.85%)
occurrences (all)	2	0	3
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	2
MUSCLE SPASMS			
subjects affected / exposed	2 / 6 (33.33%)	1 / 15 (6.67%)	6 / 78 (7.69%)
occurrences (all)	3	1	10
LIMB DISCOMFORT			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	3 / 78 (3.85%)
occurrences (all)	0	3	3
BACK PAIN			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	14 / 78 (17.95%)
occurrences (all)	2	0	26
ARTHRALGIA			

subjects affected / exposed	3 / 6 (50.00%)	3 / 15 (20.00%)	12 / 78 (15.38%)
occurrences (all)	8	5	26
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
SPONDYLITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
HERPES ZOSTER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	5 / 78 (6.41%)
occurrences (all)	0	0	6
BRONCHITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	4 / 78 (5.13%)
occurrences (all)	0	0	5
CANDIDA INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
CELLULITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
CONJUNCTIVITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	3 / 78 (3.85%)
occurrences (all)	0	3	3
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	19 / 78 (24.36%)
occurrences (all)	1	4	22
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
CYSTITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	13	0	2
DEMODICIDOSIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0

EPIDIDYMITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
ERYSIPELAS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	2	0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
FOLLICULITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	2	2
FUNGAL INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
INFLUENZA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
NASAL ABSCESS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	4 / 78 (5.13%)
occurrences (all)	1	0	4
ORAL HERPES			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
PARONYCHIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 78 (1.28%)
occurrences (all)	2	0	1
PNEUMONIA			

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 78 (2.56%)
occurrences (all)	0	1	3
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	0	0	3
RHINITIS			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	2 / 78 (2.56%)
occurrences (all)	0	2	2
SINUSITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	2	8
SKIN CANDIDA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
TINEA CRURIS			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	9 / 78 (11.54%)
occurrences (all)	2	3	13
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 6 (16.67%)	4 / 15 (26.67%)	7 / 78 (8.97%)
occurrences (all)	4	14	21
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
LOCALISED INFECTION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 78 (2.56%)
occurrences (all)	1	0	4
WOUND INFECTION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			

HYPOKALAEMIA			
subjects affected / exposed	2 / 6 (33.33%)	5 / 15 (33.33%)	16 / 78 (20.51%)
occurrences (all)	2	11	24
HYPERVOLAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HYPERURICAEMIA			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	5 / 78 (6.41%)
occurrences (all)	3	3	5
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	9 / 78 (11.54%)
occurrences (all)	0	0	12
HYPERNATRAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HYPERKALAEMIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	8 / 78 (10.26%)
occurrences (all)	1	0	8
DEHYDRATION			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	1 / 78 (1.28%)
occurrences (all)	1	2	1
DECREASED APPETITE			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	8 / 78 (10.26%)
occurrences (all)	1	4	9
ACIDOSIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 78 (1.28%)
occurrences (all)	0	1	1
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	2	4

HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 78 (5.13%)
occurrences (all)	0	2	7
HYPONATRAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	1 / 78 (1.28%)
occurrences (all)	0	2	4
HYPOMAGNESAEMIA			
subjects affected / exposed	4 / 6 (66.67%)	3 / 15 (20.00%)	16 / 78 (20.51%)
occurrences (all)	6	5	21

Non-serious adverse events	Randomization Phase: Ibrutinib + Placebo	Randomization Phase: Ibrutinb + Venetoclax	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	127 / 132 (96.21%)	131 / 134 (97.76%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences (all)	0	2	
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
BASAL CELL CARCINOMA			
subjects affected / exposed	5 / 132 (3.79%)	7 / 134 (5.22%)	
occurrences (all)	5	10	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	4 / 132 (3.03%)	7 / 134 (5.22%)	
occurrences (all)	6	7	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
HAEMATOMA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
HYPERTENSION			

subjects affected / exposed	23 / 132 (17.42%)	20 / 134 (14.93%)	
occurrences (all)	28	32	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	4 / 132 (3.03%)	6 / 134 (4.48%)	
occurrences (all)	5	7	
ADVERSE DRUG REACTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
ASTHENIA			
subjects affected / exposed	18 / 132 (13.64%)	26 / 134 (19.40%)	
occurrences (all)	24	38	
CATHETER SITE BRUISE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
CHILLS			
subjects affected / exposed	4 / 132 (3.03%)	8 / 134 (5.97%)	
occurrences (all)	4	8	
FATIGUE			
subjects affected / exposed	36 / 132 (27.27%)	39 / 134 (29.10%)	
occurrences (all)	77	66	
GENERALISED OEDEMA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
IMPAIRED HEALING			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	5 / 132 (3.79%)	10 / 134 (7.46%)	
occurrences (all)	6	11	
INJECTION SITE BRUISING			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
NON-CARDIAC CHEST PAIN			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
OEDEMA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
OEDEMA PERIPHERAL			
subjects affected / exposed	21 / 132 (15.91%)	16 / 134 (11.94%)	
occurrences (all)	28	20	
PAIN			
subjects affected / exposed	4 / 132 (3.03%)	3 / 134 (2.24%)	
occurrences (all)	4	3	
PERIPHERAL SWELLING			
subjects affected / exposed	9 / 132 (6.82%)	11 / 134 (8.21%)	
occurrences (all)	11	19	
PYREXIA			
subjects affected / exposed	28 / 132 (21.21%)	28 / 134 (20.90%)	
occurrences (all)	56	51	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
EXTRAVASATION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	3 / 132 (2.27%)	2 / 134 (1.49%)	
occurrences (all)	4	2	
ALLERGY TO ARTHROPOD BITE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
PRODUCTIVE COUGH			
subjects affected / exposed	6 / 132 (4.55%)	5 / 134 (3.73%)	
occurrences (all)	7	8	
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
COUGH			
subjects affected / exposed	35 / 132 (26.52%)	28 / 134 (20.90%)	
occurrences (all)	55	46	
DYSPHONIA			
subjects affected / exposed	3 / 132 (2.27%)	4 / 134 (2.99%)	
occurrences (all)	3	4	
PLEURITIC PAIN			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
PLEURAL EFFUSION			
subjects affected / exposed	3 / 132 (2.27%)	4 / 134 (2.99%)	
occurrences (all)	3	4	
OROPHARYNGEAL PAIN			
subjects affected / exposed	15 / 132 (11.36%)	14 / 134 (10.45%)	
occurrences (all)	21	15	
NASAL DRYNESS			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
NASAL CONGESTION			
subjects affected / exposed	6 / 132 (4.55%)	7 / 134 (5.22%)	
occurrences (all)	6	8	
EPISTAXIS			
subjects affected / exposed	14 / 132 (10.61%)	9 / 134 (6.72%)	
occurrences (all)	23	14	
DYSPNOEA			
subjects affected / exposed	15 / 132 (11.36%)	17 / 134 (12.69%)	
occurrences (all)	24	24	
PULMONARY OEDEMA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
SINUS CONGESTION			

subjects affected / exposed	6 / 132 (4.55%)	3 / 134 (2.24%)	
occurrences (all)	7	3	
SINUS DISORDER			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	3 / 132 (2.27%)	3 / 134 (2.24%)	
occurrences (all)	3	4	
VOCAL CORD POLYP			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
WHEEZING			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences (all)	2	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	6 / 132 (4.55%)	5 / 134 (3.73%)	
occurrences (all)	7	6	
CONFUSIONAL STATE			
subjects affected / exposed	1 / 132 (0.76%)	3 / 134 (2.24%)	
occurrences (all)	1	3	
INSOMNIA			
subjects affected / exposed	13 / 132 (9.85%)	12 / 134 (8.96%)	
occurrences (all)	14	12	
DISORIENTATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
DEPRESSION			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	1	2	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 132 (2.27%)	4 / 134 (2.99%)	
occurrences (all)	5	4	
ASPARTATE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	2 / 132 (1.52%)	5 / 134 (3.73%)	
occurrences (all)	2	5	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 132 (0.76%)	4 / 134 (2.99%)	
occurrences (all)	1	7	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 132 (1.52%)	3 / 134 (2.24%)	
occurrences (all)	4	4	
BLOOD CREATININE INCREASED			
subjects affected / exposed	13 / 132 (9.85%)	7 / 134 (5.22%)	
occurrences (all)	27	8	
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences (all)	5	1	
BLOOD PRESSURE INCREASED			
subjects affected / exposed	2 / 132 (1.52%)	7 / 134 (5.22%)	
occurrences (all)	2	9	
BLOOD UREA INCREASED			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences (all)	7	0	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 132 (1.52%)	1 / 134 (0.75%)	
occurrences (all)	2	4	
WEIGHT DECREASED			
subjects affected / exposed	7 / 132 (5.30%)	15 / 134 (11.19%)	
occurrences (all)	7	17	
TROPONIN T INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
PLATELET COUNT DECREASED			

subjects affected / exposed	5 / 132 (3.79%)	3 / 134 (2.24%)	
occurrences (all)	11	3	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	5 / 132 (3.79%)	2 / 134 (1.49%)	
occurrences (all)	12	2	
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	3 / 132 (2.27%)	8 / 134 (5.97%)	
occurrences (all)	3	8	
FALL			
subjects affected / exposed	7 / 132 (5.30%)	11 / 134 (8.21%)	
occurrences (all)	7	11	
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	2	
LIMB INJURY			
subjects affected / exposed	6 / 132 (4.55%)	0 / 134 (0.00%)	
occurrences (all)	6	0	
SCRATCH			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
SKIN ABRASION			
subjects affected / exposed	0 / 132 (0.00%)	3 / 134 (2.24%)	
occurrences (all)	0	3	
SKIN LACERATION			
subjects affected / exposed	2 / 132 (1.52%)	5 / 134 (3.73%)	
occurrences (all)	2	6	
THERMAL BURN			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
TRAUMATIC HAEMATOMA			
subjects affected / exposed	5 / 132 (3.79%)	2 / 134 (1.49%)	
occurrences (all)	7	2	
Cardiac disorders			

ATRIAL FIBRILLATION			
subjects affected / exposed	12 / 132 (9.09%)	12 / 134 (8.96%)	
occurrences (all)	16	14	
BRADYCARDIA			
subjects affected / exposed	2 / 132 (1.52%)	4 / 134 (2.99%)	
occurrences (all)	2	4	
PALPITATIONS			
subjects affected / exposed	3 / 132 (2.27%)	5 / 134 (3.73%)	
occurrences (all)	3	8	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	22 / 132 (16.67%)	15 / 134 (11.19%)	
occurrences (all)	43	19	
DYSKINESIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
DYSGEUSIA			
subjects affected / exposed	2 / 132 (1.52%)	6 / 134 (4.48%)	
occurrences (all)	2	6	
DYSARTHRIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
DIZZINESS			
subjects affected / exposed	20 / 132 (15.15%)	16 / 134 (11.94%)	
occurrences (all)	35	22	
PARESIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
HYPOAESTHESIA			
subjects affected / exposed	6 / 132 (4.55%)	8 / 134 (5.97%)	
occurrences (all)	9	10	
MEMORY IMPAIRMENT			
subjects affected / exposed	4 / 132 (3.03%)	1 / 134 (0.75%)	
occurrences (all)	10	3	
NEUROPATHY PERIPHERAL			

subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
PARAESTHESIA			
subjects affected / exposed	14 / 132 (10.61%)	5 / 134 (3.73%)	
occurrences (all)	23	9	
VASCULAR ENCEPHALOPATHY			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
TREMOR			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	1	4	
SYNCOPE			
subjects affected / exposed	3 / 132 (2.27%)	6 / 134 (4.48%)	
occurrences (all)	4	7	
SENSORY DISTURBANCE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
SCIATICA			
subjects affected / exposed	3 / 132 (2.27%)	2 / 134 (1.49%)	
occurrences (all)	5	3	
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
PRESYNCOPE			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	2	2	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	7 / 132 (5.30%)	4 / 134 (2.99%)	
occurrences (all)	13	4	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	17 / 132 (12.88%)	27 / 134 (20.15%)	
occurrences (all)	32	40	
LEUKOPENIA			
subjects affected / exposed	1 / 132 (0.76%)	12 / 134 (8.96%)	
occurrences (all)	2	53	

LYMPHADENOPATHY			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	4	2	
NEUTROPENIA			
subjects affected / exposed	19 / 132 (14.39%)	46 / 134 (34.33%)	
occurrences (all)	25	207	
SPLENOMEGALY			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences (all)	2	0	
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	3 / 132 (2.27%)	3 / 134 (2.24%)	
occurrences (all)	3	3	
THROMBOCYTOPENIA			
subjects affected / exposed	20 / 132 (15.15%)	22 / 134 (16.42%)	
occurrences (all)	46	74	
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	10 / 132 (7.58%)	12 / 134 (8.96%)	
occurrences (all)	12	17	
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	1	2	
TINNITUS			
subjects affected / exposed	3 / 132 (2.27%)	4 / 134 (2.99%)	
occurrences (all)	3	4	
VERTIGO			
subjects affected / exposed	5 / 132 (3.79%)	6 / 134 (4.48%)	
occurrences (all)	5	6	
Eye disorders			
ASTIGMATISM			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
CATARACT			
subjects affected / exposed	9 / 132 (6.82%)	5 / 134 (3.73%)	
occurrences (all)	9	6	
VISUAL ACUITY REDUCED			

subjects affected / exposed	16 / 132 (12.12%)	20 / 134 (14.93%)	
occurrences (all)	32	42	
DIPLOPIA			
subjects affected / exposed	3 / 132 (2.27%)	1 / 134 (0.75%)	
occurrences (all)	5	2	
DRY EYE			
subjects affected / exposed	20 / 132 (15.15%)	18 / 134 (13.43%)	
occurrences (all)	45	25	
EYE DISCHARGE			
subjects affected / exposed	5 / 132 (3.79%)	2 / 134 (1.49%)	
occurrences (all)	5	3	
EYE IRRITATION			
subjects affected / exposed	21 / 132 (15.91%)	13 / 134 (9.70%)	
occurrences (all)	27	16	
EYE PAIN			
subjects affected / exposed	7 / 132 (5.30%)	6 / 134 (4.48%)	
occurrences (all)	10	10	
HYPERMETROPIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
LACRIMATION INCREASED			
subjects affected / exposed	16 / 132 (12.12%)	18 / 134 (13.43%)	
occurrences (all)	25	30	
MACULAR DEGENERATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
MACULOPATHY			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
OCULAR HYPERAEMIA			
subjects affected / exposed	3 / 132 (2.27%)	1 / 134 (0.75%)	
occurrences (all)	3	1	
PHOTOPHOBIA			
subjects affected / exposed	12 / 132 (9.09%)	11 / 134 (8.21%)	
occurrences (all)	19	14	
PHOTOPSIA			

subjects affected / exposed	3 / 132 (2.27%)	5 / 134 (3.73%)	
occurrences (all)	3	8	
VISION BLURRED			
subjects affected / exposed	23 / 132 (17.42%)	25 / 134 (18.66%)	
occurrences (all)	50	47	
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences (all)	3	2	
VITREOUS FLOATERS			
subjects affected / exposed	10 / 132 (7.58%)	5 / 134 (3.73%)	
occurrences (all)	12	7	
Gastrointestinal disorders			
FLATULENCE			
subjects affected / exposed	3 / 132 (2.27%)	6 / 134 (4.48%)	
occurrences (all)	3	6	
ABDOMINAL PAIN			
subjects affected / exposed	12 / 132 (9.09%)	14 / 134 (10.45%)	
occurrences (all)	17	22	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	9 / 132 (6.82%)	6 / 134 (4.48%)	
occurrences (all)	11	8	
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
APHTHOUS ULCER			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	9	2	
CHRONIC GASTRITIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
CONSTIPATION			
subjects affected / exposed	23 / 132 (17.42%)	19 / 134 (14.18%)	
occurrences (all)	59	23	
DIARRHOEA			
subjects affected / exposed	48 / 132 (36.36%)	84 / 134 (62.69%)	
occurrences (all)	89	243	

DRY MOUTH			
subjects affected / exposed	10 / 132 (7.58%)	7 / 134 (5.22%)	
occurrences (all)	11	9	
DUODENITIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences (all)	0	2	
DYSPEPSIA			
subjects affected / exposed	11 / 132 (8.33%)	19 / 134 (14.18%)	
occurrences (all)	13	28	
DYSPHAGIA			
subjects affected / exposed	3 / 132 (2.27%)	3 / 134 (2.24%)	
occurrences (all)	7	5	
ENTERITIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
FAECES SOFT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
FEMORAL HERNIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
ABDOMINAL DISTENSION			
subjects affected / exposed	4 / 132 (3.03%)	4 / 134 (2.99%)	
occurrences (all)	4	4	
GASTRITIS			
subjects affected / exposed	5 / 132 (3.79%)	7 / 134 (5.22%)	
occurrences (all)	6	8	
GLOSSODYNIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
HAEMORRHOIDS			
subjects affected / exposed	3 / 132 (2.27%)	7 / 134 (5.22%)	
occurrences (all)	3	10	
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	

MOUTH ULCERATION			
subjects affected / exposed	6 / 132 (4.55%)	11 / 134 (8.21%)	
occurrences (all)	6	15	
NAUSEA			
subjects affected / exposed	21 / 132 (15.91%)	43 / 134 (32.09%)	
occurrences (all)	36	78	
OESOPHAGITIS			
subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences (all)	2	2	
PEPTIC ULCER			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
STOMATITIS			
subjects affected / exposed	11 / 132 (8.33%)	12 / 134 (8.96%)	
occurrences (all)	20	16	
TONGUE ERYTHEMA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
TONGUE HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
TOOTHACHE			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
VOMITING			
subjects affected / exposed	14 / 132 (10.61%)	27 / 134 (20.15%)	
occurrences (all)	24	59	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	5 / 132 (3.79%)	11 / 134 (8.21%)	
occurrences (all)	5	15	
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	3 / 134 (2.24%)	
occurrences (all)	1	7	
HEPATIC FUNCTION ABNORMAL			

subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences (all)	3	10	
HEPATITIS CHOLESTATIC			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
PORTAL FIBROSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
ONYCHOCLASIS			
subjects affected / exposed	7 / 132 (5.30%)	11 / 134 (8.21%)	
occurrences (all)	9	13	
PETECHIAE			
subjects affected / exposed	5 / 132 (3.79%)	6 / 134 (4.48%)	
occurrences (all)	10	8	
ALOPECIA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
BLOOD BLISTER			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
DECUBITUS ULCER			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
DRY SKIN			
subjects affected / exposed	5 / 132 (3.79%)	6 / 134 (4.48%)	
occurrences (all)	5	7	
ECCHYMOSIS			
subjects affected / exposed	2 / 132 (1.52%)	2 / 134 (1.49%)	
occurrences (all)	2	2	
ERYTHEMA			
subjects affected / exposed	3 / 132 (2.27%)	7 / 134 (5.22%)	
occurrences (all)	3	8	

HYPERHIDROSIS			
subjects affected / exposed	4 / 132 (3.03%)	1 / 134 (0.75%)	
occurrences (all)	6	1	
NIGHT SWEATS			
subjects affected / exposed	5 / 132 (3.79%)	9 / 134 (6.72%)	
occurrences (all)	6	10	
PRURITUS			
subjects affected / exposed	15 / 132 (11.36%)	15 / 134 (11.19%)	
occurrences (all)	26	18	
RASH			
subjects affected / exposed	2 / 132 (1.52%)	5 / 134 (3.73%)	
occurrences (all)	3	7	
RASH ERYTHEMATOUS			
subjects affected / exposed	5 / 132 (3.79%)	8 / 134 (5.97%)	
occurrences (all)	6	9	
RASH MACULO-PAPULAR			
subjects affected / exposed	12 / 132 (9.09%)	18 / 134 (13.43%)	
occurrences (all)	14	33	
SKIN LESION			
subjects affected / exposed	1 / 132 (0.76%)	4 / 134 (2.99%)	
occurrences (all)	1	7	
URTICARIA			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences (all)	0	2	
SKIN ULCER			
subjects affected / exposed	1 / 132 (0.76%)	5 / 134 (3.73%)	
occurrences (all)	2	6	
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	4 / 132 (3.03%)	5 / 134 (3.73%)	
occurrences (all)	5	7	
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences (all)	2	0	
BLADDER HYPERTROPHY			

subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 132 (2.27%)	1 / 134 (0.75%)	
occurrences (all)	4	2	
HAEMATURIA			
subjects affected / exposed	5 / 132 (3.79%)	4 / 134 (2.99%)	
occurrences (all)	7	5	
POLLAKIURIA			
subjects affected / exposed	2 / 132 (1.52%)	4 / 134 (2.99%)	
occurrences (all)	2	4	
RENAL FAILURE			
subjects affected / exposed	2 / 132 (1.52%)	3 / 134 (2.24%)	
occurrences (all)	3	5	
URINARY INCONTINENCE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	2	
URINARY RETENTION			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	4	3	
NEPHROLITHIASIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	12 / 132 (9.09%)	11 / 134 (8.21%)	
occurrences (all)	18	18	
OSTEOARTHRITIS			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	4	2	
NECK PAIN			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	4	2	
MYALGIA			

subjects affected / exposed	17 / 132 (12.88%)	13 / 134 (9.70%)	
occurrences (all)	34	18	
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 132 (0.76%)	6 / 134 (4.48%)	
occurrences (all)	5	7	
MUSCLE SPASMS			
subjects affected / exposed	32 / 132 (24.24%)	12 / 134 (8.96%)	
occurrences (all)	56	16	
LIMB DISCOMFORT			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
JOINT SWELLING			
subjects affected / exposed	4 / 132 (3.03%)	4 / 134 (2.99%)	
occurrences (all)	10	6	
BACK PAIN			
subjects affected / exposed	15 / 132 (11.36%)	12 / 134 (8.96%)	
occurrences (all)	20	18	
ARTHRALGIA			
subjects affected / exposed	23 / 132 (17.42%)	22 / 134 (16.42%)	
occurrences (all)	47	29	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	2	0	
SPONDYLITIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
HERPES ZOSTER			
subjects affected / exposed	8 / 132 (6.06%)	3 / 134 (2.24%)	
occurrences (all)	10	3	
BRONCHITIS			
subjects affected / exposed	9 / 132 (6.82%)	7 / 134 (5.22%)	
occurrences (all)	15	10	

CANDIDA INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
CELLULITIS			
subjects affected / exposed	0 / 132 (0.00%)	7 / 134 (5.22%)	
occurrences (all)	0	10	
CONJUNCTIVITIS			
subjects affected / exposed	11 / 132 (8.33%)	8 / 134 (5.97%)	
occurrences (all)	15	10	
COVID-19			
subjects affected / exposed	16 / 132 (12.12%)	16 / 134 (11.94%)	
occurrences (all)	22	20	
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
CYSTITIS			
subjects affected / exposed	5 / 132 (3.79%)	2 / 134 (1.49%)	
occurrences (all)	5	3	
DEMODICIDOSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
EPIDIDYMITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
ERYSIPELAS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	1 / 134 (0.75%)	
occurrences (all)	1	1	
FOLLICULITIS			
subjects affected / exposed	1 / 132 (0.76%)	3 / 134 (2.24%)	
occurrences (all)	1	4	
FUNGAL INFECTION			

subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
INFLUENZA			
subjects affected / exposed	2 / 132 (1.52%)	7 / 134 (5.22%)	
occurrences (all)	2	12	
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
NASAL ABSCESS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
NASOPHARYNGITIS			
subjects affected / exposed	8 / 132 (6.06%)	8 / 134 (5.97%)	
occurrences (all)	9	11	
ORAL HERPES			
subjects affected / exposed	7 / 132 (5.30%)	8 / 134 (5.97%)	
occurrences (all)	9	10	
PARONYCHIA			
subjects affected / exposed	7 / 132 (5.30%)	5 / 134 (3.73%)	
occurrences (all)	12	6	
PNEUMONIA			
subjects affected / exposed	7 / 132 (5.30%)	7 / 134 (5.22%)	
occurrences (all)	9	7	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	7 / 132 (5.30%)	6 / 134 (4.48%)	
occurrences (all)	18	11	
RHINITIS			
subjects affected / exposed	9 / 132 (6.82%)	3 / 134 (2.24%)	
occurrences (all)	10	3	
SINUSITIS			
subjects affected / exposed	6 / 132 (4.55%)	11 / 134 (8.21%)	
occurrences (all)	8	14	
SKIN CANDIDA			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
TINEA CRURIS			

subjects affected / exposed	1 / 132 (0.76%)	0 / 134 (0.00%)	
occurrences (all)	1	0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	14 / 132 (10.61%)	23 / 134 (17.16%)	
occurrences (all)	16	42	
URINARY TRACT INFECTION			
subjects affected / exposed	10 / 132 (7.58%)	14 / 134 (10.45%)	
occurrences (all)	12	22	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	2 / 134 (1.49%)	
occurrences (all)	0	4	
LOCALISED INFECTION			
subjects affected / exposed	1 / 132 (0.76%)	5 / 134 (3.73%)	
occurrences (all)	1	8	
WOUND INFECTION			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
HYPOKALAEMIA			
subjects affected / exposed	8 / 132 (6.06%)	21 / 134 (15.67%)	
occurrences (all)	13	31	
HYPERVOLAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 134 (0.75%)	
occurrences (all)	0	1	
HYPERURICAEMIA			
subjects affected / exposed	11 / 132 (8.33%)	9 / 134 (6.72%)	
occurrences (all)	15	12	
HYPERPHOSPHATAEMIA			
subjects affected / exposed	3 / 132 (2.27%)	2 / 134 (1.49%)	
occurrences (all)	3	3	
HYPERNATRAEMIA			
subjects affected / exposed	2 / 132 (1.52%)	0 / 134 (0.00%)	
occurrences (all)	3	0	
HYPERKALAEMIA			

subjects affected / exposed	3 / 132 (2.27%)	5 / 134 (3.73%)	
occurrences (all)	4	5	
DEHYDRATION			
subjects affected / exposed	4 / 132 (3.03%)	4 / 134 (2.99%)	
occurrences (all)	4	4	
DECREASED APPETITE			
subjects affected / exposed	15 / 132 (11.36%)	24 / 134 (17.91%)	
occurrences (all)	18	33	
ACIDOSIS			
subjects affected / exposed	0 / 132 (0.00%)	0 / 134 (0.00%)	
occurrences (all)	0	0	
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	1	2	
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	1 / 132 (0.76%)	2 / 134 (1.49%)	
occurrences (all)	1	2	
IRON DEFICIENCY			
subjects affected / exposed	3 / 132 (2.27%)	4 / 134 (2.99%)	
occurrences (all)	3	5	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	4 / 132 (3.03%)	4 / 134 (2.99%)	
occurrences (all)	6	5	
HYPONATRAEMIA			
subjects affected / exposed	4 / 132 (3.03%)	2 / 134 (1.49%)	
occurrences (all)	5	3	
HYPOMAGNESAEMIA			
subjects affected / exposed	4 / 132 (3.03%)	14 / 134 (10.45%)	
occurrences (all)	13	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2017	• Included 560 mg tablet to decrease the pill burden for subjects participating in the study • Included that a prior rituximab/anti-CD20-containing regimen was required • Extended the ECOG performance status to include subjects with ECOG performance status of 2 in order to expand study eligibility to a broader population of subjects • Updated the ibrutinib and venetoclax overview and safety sections according to current IB version and labeling information • Updated the rationale for ibrutinib and venetoclax combination to include current results and reference based on ICML 2017 data • Excluded subjects who could not tolerate study treatment due to hypersensitivity to 1 or more study drug components • Included a 24-hour time window for the investigator to notify the sponsor in case subject discontinued study treatment.
07 November 2019	• Removed the planned Interim Analysis for the SRI and Randomization Phase • Added the treatment-naive arm, including subjects with a TP53 mutation • Added the rationale for the treatment-naive arm, including subjects with a TP53 mutation • Removed the now obsolete ibrutinib Lead-in Schedule of treatment • Added further clarity regarding the maximum dose of ibrutinib tablets and capsules.
25 March 2021	• Changed eligibility to adults ≥ 18 years with a TP53 mutation for the treatment naive cohort • Removed the requirement of 25 subjects less than 65 years of age with a TP53 mutation • Updated the MRD analysis population • Added the OS assumptions • Added an interim analysis for OS at the time of the primary analysis for PFS at 134 events • Added cardiac failure as a risk per IB update • Clarified that dose reductions are an option to manage Grade 2 AEs • Removed required sequencing of PET first then CT if on the same day • Clarification that only post-dose laboratory assessments will be considered for TLS when applying Howard Criteria • Made corrections regarding MRD testing in text and schedule of activities (SoA).
16 September 2022	• Included updated recommendations intended to improve tolerability for continued ibrutinib treatment in the study protocol • Included a new Protocol Table 2: Ibrutinib Dose Modifications for Cardiac Failure or Cardiac Arrhythmias • Clarified that all patients need to have adequate response assessments per schedule of assessment until the end of study • Clarified that all patients need to have adequate patient-reported outcomes per schedule of assessments until the end of study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported