



Clinical trial results:

Phase 2 Study of the Combination of Ibrutinib Plus Venetoclax in Subjects With Treatment-naïve Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Summary

EudraCT number	2016-002293-12
Trial protocol	ES IT
Global end of trial date	27 March 2024

Results information

Result version number	v1 (current)
This version publication date	11 December 2024
First version publication date	11 December 2024

Trial information

Trial identification

Sponsor protocol code	PCYC-1142-CA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02910583
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pharmacyclics LLC
Sponsor organisation address	1000 Gateway Boulevard, South San Francisco, United States, 94080
Public contact	Global Medical Services, AbbVie, 001 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 001 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 March 2024
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

This is a multicenter, 2-cohort Phase 2 study assessing both minimal residual disease (MRD)-guided discontinuation and fixed duration therapy with the combination of ibrutinib + venetoclax in subjects with treatment-naïve CLL or SLL.

Protection of trial subjects:

The study was conducted in accordance with the protocol ICH guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 77
Country: Number of subjects enrolled	Italy: 39
Country: Number of subjects enrolled	New Zealand: 21
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	United States: 147
Worldwide total number of subjects	323
EEA total number of subjects	78

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)	237
From 65 to 84 years	86
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 39 centers in the United States (US), Australia, New Zealand, Spain, and Italy.

Pre-assignment

Screening details:

Upon completion of a pre-randomization phase, participants in the MRD Cohort with confirmed undetectable minimal residual disease (uMRD) were randomized to blinded ibrutinib or placebo. Subjects in the MRD Cohort with uMRD not confirmed were randomized to open-label ibrutinib or open-label ibrutinib + venetoclax.

Period 1

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

Blinding implementation details:

Triple (Participant, Investigator, Outcomes Assessor)

Participants with confirmed undetectable minimal residual disease (uMRD) in the MRD cohort are triple masked.

Allocation was not randomized for the Fixed Duration (FD) cohort.

Arms

Are arms mutually exclusive?	Yes
Arm title	Fixed Duration (FD) Cohort: All Treated

Arm description:

Subjects received 420mg Ibrutinib (IBR) for 3 cycles followed by combination treatment with IBR 420mg and Venetoclax (VEN) 400mg orally once daily on a continuous schedule for 12 cycles (1 cycle=28 days) or until disease progression or unacceptable toxicity, whichever was earlier. Subjects with confirmed progression per 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria after completing the FD regimen could be retreated with continuous single agent IBR until disease progression or unacceptable toxicity, whichever was earlier, because it is an established standard of care for relapsed chronic lymphocytic leukemia (CLL). For subjects with durable efficacy after IBR plus VEN (ie, time to progression after FD regimen is completed of >2 years), the IBR plus VEN FD treatment regimen may have been repeated based on Investigator's clinical discretion and Medical Monitor's approval. Retreatment was for 15 cycles, until disease progression or unacceptable toxicity.

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

Dosage and administration details:

Ibrutinib administered orally once daily (three 140 mg capsules)

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

Dosage and administration details:

Venetoclax tablets will be administered orally once daily starting with a 5 week ramp up of 20 mg, 50 mg, 100 mg, 200 mg and 400 mg. After ramp up, venetoclax will be administered at 400 mg.

Arm title	Minimal Residual Disease (MRD) Cohort: All Treated
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Arm description:

Subjects received 420mg of single-agent Ibrutinib (IBR) for the first 3 cycles followed by IBR plus Venetoclax (VEN) combination treatment for at least 12 cycles (1 cycle=28 days) prior to randomization (pre-randomization phase). Subjects who completed the planned pre-randomization treatment are eligible to be randomized according to their confirmed undetectable minimal residual disease (uMRD) status: Subjects with confirmed uMRD were randomized to receive blinded IBR 420mg or placebo orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. Subjects with uMRD not confirmed were randomized to receive open-label IBR 420mg or open-label IBR 420mg plus VEN 400mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. The VEN could be administered cumulative from pre-randomization to randomization phase at the dose of 400mg/day for up to approximately 2 years, or earlier PD or unacceptable toxicity.

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

Dosage and administration details:

Ibrutinib administered orally once daily (three 140 mg capsules)

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

Dosage and administration details:

Venetoclax tablets will be administered orally once daily starting with a 5 week ramp up of 20 mg, 50 mg, 100 mg, 200 mg and 400 mg. After ramp up, venetoclax will be administered at 400 mg.

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

Dosage and administration details:

Placebo capsules to match ibrutinib administered orally once daily

Number of subjects in period 1	Fixed Duration (FD) Cohort: All Treated	Minimal Residual Disease (MRD) Cohort: All Treated
Started	159	164
Completed	133	150
Not completed	26	14
Consent withdrawn by subject	12	8
Death	7	3
Not Specified	6	3
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Fixed Duration (FD) Cohort: All Treated
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Reporting group description:

Subjects received 420mg Ibrutinib (IBR) for 3 cycles followed by combination treatment with IBR 420mg and Venetoclax (VEN) 400mg orally once daily on a continuous schedule for 12 cycles (1 cycle=28 days) or until disease progression or unacceptable toxicity, whichever was earlier. Subjects with confirmed progression per 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria after completing the FD regimen could be retreated with continuous single agent IBR until disease progression or unacceptable toxicity, whichever was earlier, because it is an established standard of care for relapsed chronic lymphocytic leukemia (CLL). For subjects with durable efficacy after IBR plus VEN (ie, time to progression after FD regimen is completed of >2 years), the IBR plus VEN FD treatment regimen may have been repeated based on Investigator's clinical discretion and Medical Monitor's approval. Retreatment was for 15 cycles, until disease progression or unacceptable toxicity.

Reporting group title	Minimal Residual Disease (MRD) Cohort: All Treated
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Reporting group description:

Subjects received 420mg of single-agent Ibrutinib (IBR) for the first 3 cycles followed by IBR plus Venetoclax (VEN) combination treatment for at least 12 cycles (1 cycle=28 days) prior to randomization (pre-randomization phase). Subjects who completed the planned pre-randomization treatment are eligible to be randomized according to their confirmed undetectable minimal residual disease (uMRD) status: Subjects with confirmed uMRD were randomized to receive blinded IBR 420mg or placebo orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. Subjects with uMRD not confirmed were randomized to receive open-label IBR 420mg or open-label IBR 420mg plus VEN 400mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. The VEN could be administered cumulative from pre-randomization to randomization phase at the dose of 400mg/day for up to approximately 2 years, or earlier PD or unacceptable toxicity.

Reporting group values	Fixed Duration (FD) Cohort: All Treated	Minimal Residual Disease (MRD) Cohort: All Treated	Total
Number of subjects	159	164	323
Age categorical Units: Subjects			
<65	114	123	237
>=65	45	41	86
Gender categorical Units: Subjects			
Female	53	61	114
Male	106	103	209
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	5	11	16
Not Hispanic or Latino	149	150	299
Unknown or Not Reported	5	3	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	5	8
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	1	2	3
White	147	147	294
More than one race	0	0	0
Unknown or Not Reported	7	9	16

End points

End points reporting groups

Reporting group title	Fixed Duration (FD) Cohort: All Treated
Reporting group description:	
Subjects received 420mg Ibrutinib (IBR) for 3 cycles followed by combination treatment with IBR 420mg and Venetoclax (VEN) 400mg orally once daily on a continuous schedule for 12 cycles (1 cycle=28 days) or until disease progression or unacceptable toxicity, whichever was earlier. Subjects with confirmed progression per 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria after completing the FD regimen could be retreated with continuous single agent IBR until disease progression or unacceptable toxicity, whichever was earlier, because it is an established standard of care for relapsed chronic lymphocytic leukemia (CLL). For subjects with durable efficacy after IBR plus VEN (ie, time to progression after FD regimen is completed of >2 years), the IBR plus VEN FD treatment regimen may have been repeated based on Investigator's clinical discretion and Medical Monitor's approval. Retreatment was for 15 cycles, until disease progression or unacceptable toxicity.	
Reporting group title	Minimal Residual Disease (MRD) Cohort: All Treated
Reporting group description:	
Subjects received 420mg of single-agent Ibrutinib (IBR) for the first 3 cycles followed by IBR plus Venetoclax (VEN) combination treatment for at least 12 cycles (1 cycle=28 days) prior to randomization (pre-randomization phase). Subjects who completed the planned pre-randomization treatment are eligible to be randomized according to their confirmed undetectable minimal residual disease (uMRD) status: Subjects with confirmed uMRD were randomized to receive blinded IBR 420mg or placebo orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. Subjects with uMRD not confirmed were randomized to receive open-label IBR 420mg or open-label IBR 420mg plus VEN 400mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. The VEN could be administered cumulative from pre-randomization to randomization phase at the dose of 400mg/day for up to approximately 2 years, or earlier PD or unacceptable toxicity.	
Subject analysis set title	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects receive venetoclax combination treatment for at least 12 cycles (a cycle is defined as 28 days) prior to randomization (pre-randomization phase). Subjects with confirmed uMRD are randomized to receive ibrutinib 420 mg orally once daily on a continuous schedule until MRD-positive relapse, disease progression (PD), or unacceptable toxicity, whichever was earlier. After MRD-positive relapse or disease progression (PD) by iwCLL criteria, subjects can reintroduce 400 mg venetoclax with a 5-week ramp up. If venetoclax is to be reintroduced, venetoclax treatment is to continue at the dose of 400 mg/day for up to approximately 2 years (cumulative), or earlier PD or unacceptable toxicity.	
Subject analysis set title	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects receive 420 mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (a cycle is defined as 28 days) prior to randomization (pre-randomization phase). Subjects with confirmed uMRD are randomized to receive placebo orally once daily on a continuous schedule until MRD-positive relapse, PD or unacceptable toxicity, whichever was earlier. If MRD-positive relapse or PD is confirmed after restaging per iwCLL criteria, subjects can first reintroduce oral daily ibrutinib with the option of subsequently reintroducing 400 mg venetoclax with a 5-week ramp up, if subsequent disease relapse per iwCLL criteria occurs after ibrutinib reintroduction. If venetoclax is to be reintroduced, venetoclax treatment is to continue at the dose of 400 mg/day for up to approximately 2 years (cumulative), or earlier PD or unacceptable toxicity.	
Subject analysis set title	MRD/uMRD Not Confirmed: All Treated
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received 420 mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (a cycle is defined as 28 days) prior to randomization (pre-randomization phase). Subjects with uMRD not confirmed were randomized to receive open-label ibrutinib 420 mg or open-label ibrutinib 420 mg plus venetoclax 400 mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier.	
Subject analysis set title	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 420 mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (a cycle is defined as 28 days) prior to randomization (pre-randomization phase). Subjects with uMRD not confirmed were randomized to receive open-label ibrutinib 420 mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. In case of confirmed PD after restaging per iwCLL criteria, subjects can continue ibrutinib and reintroduce venetoclax treatment. If venetoclax is to be reintroduced, venetoclax treatment is to continue at the dose of 400 mg/day for up to approximately 2 years (cumulative) or earlier PD or unacceptable toxicity.

Subject analysis set title	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 420 mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (a cycle is defined as 28 days) prior to randomization (pre-randomization phase). Subjects with uMRD not confirmed were randomized to receive open-label ibrutinib 420 mg and venetoclax 400 mg orally once daily on a continuous schedule until PD or unacceptable toxicity, whichever was earlier. In case of confirmed PD after restaging per iwCLL criteria, subjects can continue ibrutinib and reintroduce venetoclax treatment. If venetoclax is to be reintroduced, venetoclax treatment is to continue at the dose of 400 mg/day for up to approximately 2 years (cumulative) or earlier PD or unacceptable toxicity.

Subject analysis set title	FD Cohort/Non-Del 17p Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in the FD cohort without del 17p abnormality (according to non-missing baseline fluorescent in situ hybridization [FISH] results) received 420 mg of single agent ibrutinib for first 3 cycles followed by ibrutinib plus venetoclax combination treatment (ibrutinib 420 mg and venetoclax 400 mg orally once daily on a continuous schedule) for 12 cycles (a cycle is defined by 28 days) or until PD or unacceptable toxicity, whichever was earlier.

Primary: MRD Cohort: 1-Year Disease-Free Survival (DFS) Rate in Confirmed uMRD Randomized Participants

End point title	MRD Cohort: 1-Year Disease-Free Survival (DFS) Rate in Confirmed uMRD Randomized Participants
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End point description:

DFS is defined as time from randomization date to MRD-positive relapse, or disease progression per investigator assessment (per 2008 International Workshop for Chronic Lymphocytic Leukemia [IWCLL] criteria [Halleck et al]) or death from any cause, whichever occurred first. 1-year DFS estimated using Kaplan-Meier method at 12 months landmark time.

Confirmed uMRD Randomized Population: all participants who achieved confirmed MRD-negative clinical response at the end of the pre-randomization phase, randomized to either blinded placebo arm or blinded ibrutinib arm.

End point type	Primary
End point timeframe:	1 year after randomization

End point values	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	43		
Units: percentage of subjects				
number (confidence interval 95%)	100 (100 to 100)	95.3 (82.7 to 98.8)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded) v MRD/uMRD Confirmed: Randomized to Placebo (Blinded)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1475 ^[1]
Method	Z test
Parameter estimate	Difference in Rates (ibrutinib vs. PBO)
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	10.9

Notes:

[1] - P-value is from Z test for the difference of two proportions based on Kaplan-Meier estimates with standard error of each arm computed using Greenwood's formula.

Primary: FD Cohort: Complete Response Rate (CRR; Complete Response/Complete Response With Incomplete Blood Count Recovery [CR/CRi]) Rate

End point title	FD Cohort: Complete Response Rate (CRR; Complete Response/Complete Response With Incomplete Blood Count Recovery [CR/CRi]) Rate ^[2]
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End point description:

CR/CRi rate is defined as the percentage of participants achieving a best overall response of complete response (CR), CR with incomplete blood count recovery (CRi) per 2008 IWCLL criteria (halleck et al.) on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurred earlier.

Per protocol, the primary analysis of the primary endpoint for the FD cohort was based on the FD Cohort, Non-Del 17p Population only.

End point type	Primary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD, for a median follow-up of 69.0 months.

Notes:

[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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	159	136		
Units: percentage of subjects				
number (confidence interval 95%)	57.2 (49.5 to	58.1 (49.8 to		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Fixed Duration (FD) Cohort: All Treated v FD Cohort/Non-Del 17p Population
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[3]
Method	asymptotic test for binomial proportion

Notes:

[3] - One-sided P-value from asymptotic test for the binomial proportion (CRR ≤ 37% vs CRR > 37%).

Secondary: MRD Cohort: CRR (CR/CRi Rate)

End point title	MRD Cohort: CRR (CR/CRi Rate) ^[4]
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End point description:

CR/CRi rate is defined as the percentage of participants achieving a best overall response of CR or CRi per 2008 IWCLL criteria (Halleck et al.) on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurred earlier.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD Ibrutinib arm 69.1 months; Confirmed uMRD Placebo arm 67.4 months; uMRD Not Confirmed Ibrutinib arm 47.9 months; uMRD Not Confirmed Ibrutinib + Venetoclax arm 47.9 months.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

Notes:

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

Justification: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	43	43	31
Units: percentage of subjects				
number (confidence interval 95%)	66.5 (59.2 to 73.7)	79.1 (66.9 to 91.2)	65.1 (50.9 to 79.4)	77.4 (62.7 to 92.1)

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib +			
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	Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	56.3 (39.1 to 73.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Overall Response Rate (ORR)

End point title	MRD Cohort: Overall Response Rate (ORR) ^[5]
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End point description:

ORR, defined as the percentage of participants achieving a best overall response of protocol-specified complete response (CR), CR with incomplete blood count recovery (CRi), nodular partial response (nPR), partial response (PR), or PR with lymphocytosis (PRL) evaluated in accordance with the 2008 IWCLL criteria (Halleck et al). Participants who did not have any postbaseline response assessment were considered as non-responders. This table is based on response assessments performed on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurs earlier. Kaplan-Meier estimate.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD Ibrutinib arm 69.1 months; Confirmed uMRD Placebo arm 67.4 months; uMRD Not Confirmed Ibrutinib arm 47.9 months; uMRD Not Confirmed Ibrutinib + Venetoclax arm 47.9 months.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	43	43	31
Units: percentage of subjects				
number (confidence interval 95%)	97.0 (94.3 to 99.6)	100 (100 to 100)	100 (100 to 100)	100 (100 to 100)

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: percentage of subjects				

number (confidence interval 95%)	100 (100 to 100)			
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Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Duration of Response (DOR) at 42 Months Landmark Time

End point title	MRD Cohort: Duration of Response (DOR) at 42 Months Landmark Time ^[6]
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End point description:

Duration of response was calculated for participants achieving a response (CR, CRi, nPR, PR) based on 2008 IWCLL response criteria (Halleck et al.) and defined as the interval between the date of initial documentation of a response including PR with lymphocytosis, until disease progression (PD) or death from any cause, whichever occurred first. As the median DOR was not reached as of 67.0 months study follow-up, the Kaplan-Meier estimate of DOR at 42 months landmark time was presented.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD Ibrutinib arm 69.1 months; Confirmed uMRD Placebo arm 67.4 months; uMRD Not Confirmed Ibrutinib arm 47.9 months; uMRD Not Confirmed Ibrutinib + Venetoclax arm 47.9 months.

MRD Cohort: Participants who achieved PR or better

End point type	Secondary
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End point timeframe:

From initial documentation of a response until PD or death from any cause, whichever occurs first, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

Notes:

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

Justification: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	159	43	43	31
Units: Months				
number (confidence interval 95%)	93.5 (88.2 to 96.4)	97.6 (84.3 to 99.7)	93.0 (79.7 to 97.7)	96.7 (78.6 to 99.5)

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Months				
number (confidence interval 95%)	93.2 (75.5 to			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: MRD-Negativity Rate

End point title	MRD Cohort: MRD-Negativity Rate ^[7]
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End point description:

MRD negativity rate is defined as the percentage of participants achieving MRD negativity, which is defined as <1 CLL cell per 10,000 leukocytes ($<1 \times 10^{-4}$) as assessed by flow cytometry of a peripheral blood (PB) or bone marrow (BM) aspirate sample per central laboratory on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurs earlier.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD Ibrutinib arm 69.1 months; Confirmed uMRD Placebo arm 67.4 months; uMRD Not Confirmed Ibrutinib arm 47.9 months; uMRD Not Confirmed Ibrutinib + Venetoclax arm 47.9 months.

MRD All Treated Population; participants with an assessment.

End point type	Secondary
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End point timeframe:

From randomization date until before any subsequent antineoplastic therapy, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Not Confirmed: All Treated	MRD/uMRD Not Confirmed: Open-Label Ibrutinib	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	63	31	32
Units: percentage of subjects				
number (confidence interval 95%)				
PB or BM	81.7 (75.8 to 87.6)	65.1 (53.3 to 76.9)	51.6 (34.0 to 69.2)	78.1 (63.8 to 92.4)
BM	77.4 (71.0 to 83.8)	55.6 (43.3 to 67.8)	41.9 (24.6 to 59.3)	68.8 (52.7 to 84.8)
PB	79.9 (73.7 to 86.0)	60.3 (48.2 to 72.4)	48.4 (30.8 to 66.0)	71.9 (56.3 to 87.5)

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Tumor Lysis Syndrome (TLS) Risk Reduction Rate With 3-Cycle Ibrutinib Lead-In (Percentage of Participants No Longer High Risk After 3-cycle Lead-in)

End point title	MRD Cohort: Tumor Lysis Syndrome (TLS) Risk Reduction Rate With 3-Cycle Ibrutinib Lead-In (Percentage of Participants No Longer High Risk After 3-cycle Lead-in) ^[8]
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End point description:

TLS risk reduction was summarized by the percentage of participants with TLS risk reduced from high at baseline to medium or low after ibrutinib lead-in. A reduction in TLS risk from high risk to medium or low risk is clinically meaningful because there is a reduction in the extent of TLS monitoring and risk of hospitalization. TLS risk category is defined as the tumor burden category, where: Low=All lymph nodes (LN) < 5 cm AND absolute lymphocyte count (ALC) < 25 x 10⁹/L; Medium=Any LN 5 cm to < 10 cm OR ALC ≥ 25 x 10⁹/L; High=Any LN ≥ 10 cm OR ALC ≥ 25 x 10⁹/L AND any LN ≥ 5 cm.

End point type	Secondary
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End point timeframe:

Baseline, and last post-baseline value on or prior to venetoclax first dose date (cycle 4 day 1) or, for participants who never received venetoclax, the post-baseline value closest to cycle 4 day 1 (i.e. 84 days after the first dose date of ibrutinib).

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	40 ^[9]			
Units: percentage of subjects				
number (not applicable)	90.0			

Notes:

[9] - MRD Cohort: All Treated Population with baseline TLS high risk

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Kaplan-Meier Estimate of Progression Free Survival (PFS) Rate at 48 Months Landmark Time

End point title	MRD Cohort: Kaplan-Meier Estimate of Progression Free Survival (PFS) Rate at 48 Months Landmark Time ^[10]
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End point description:

PFS was defined as time from the first dose date of study treatment until disease progression (PD) or death from any cause, whichever occurs first. Assessment of PD was conducted in accordance with the 2008 IWCLL criteria (Halleck et al). As the median PFS was not reached as of the overall median 67.0 months study follow-up, the Kaplan-Meier estimate of PFS rate at 48 months landmark time was presented.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD Ibrutinib arm 69.1 months; Confirmed uMRD Placebo arm 67.4 months; uMRD Not Confirmed Ibrutinib arm 47.9 months; uMRD Not Confirmed Ibrutinib + Venetoclax arm 47.9 months.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD or death, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

Notes:

[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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	43	43	31
Units: percentage of subjects				
number (confidence interval 95%)	90.9 (85.1 to 94.5)	97.6 (84.3 to 99.7)	88.2 (73.9 to 94.9)	93.3 (75.9 to 98.3)

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	93.2 (75.5 to 98.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Kaplan-Meier Estimate of Overall Survival (OS) Rate at 48 Months Landmark Time

End point title	MRD Cohort: Kaplan-Meier Estimate of Overall Survival (OS) Rate at 48 Months Landmark Time ^[11]
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End point description:

OS is defined as the time from the first dose date of study treatment until date of death due to any cause. As the median OS was not reached as of the overall median 67.0 months study follow-up, the Kaplan-Meier estimate of OS rate at 48 months landmark time was presented.

Median follow up duration for the individual MRD Cohort treatment arms: Confirmed uMRD: Randomized to Ibrutinib=69.1 months; Confirmed uMRD: Randomized to Placebo=67.4 months; uMRD Not Confirmed: Randomized to Open-Label Ibrutinib=47.9 months; uMRD Not Confirmed: Randomized to Open-Label Ibrutinib + Venetoclax=47.9 months.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to time of death, for an overall median follow-up of 67.0 months. (Median follow up duration for the individual MRD Cohort treatment arms listed above.)

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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	43	43	31
Units: percentage of subjects				
number (confidence interval 95%)	98.0 (94.0 to 99.4)	97.6 (84.3 to 99.7)	100 (100 to 100)	96.7 (78.6 to 99.5)

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	100 (100 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs), and Discontinuations Due to TEAEs

End point title	MRD Cohort: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs), and Discontinuations Due to TEAEs ^[12]
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End point description:

An adverse event (AE) is any untoward medical occurrence, which does not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) is any untoward medical occurrence that at any dose: results in death; is life-threatening; requires unplanned in-patient hospitalization >24 hours or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event. Severity of events were graded according to the Common Terminology Criteria for Adverse Events version 4.03: mild=grade 1, moderate=grade 2, severe=grade 3, life-threatening=grade 4, death=grade 5. Causal relation of study drug and event was assessed as not related, unlikely, possibly or probably related to the study drug.

End point type	Secondary
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End point timeframe:

From first dose until 30 days following last dose of study drug. Overall treatment duration for the MRD cohort was 45.1 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated	MRD/uMRD Confirmed: Randomized to Ibrutinib (Blinded)	MRD/uMRD Confirmed: Randomized to Placebo (Blinded)	MRD/uMRD Not Confirmed: Open-Label Ibrutinib
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164	43	43	31
Units: percentage of subjects				
number (not applicable)				
Any TEAE	100.0	100.0	100.0	100.0
Any Grade ≥ 3 TEAE	75.6	83.7	72.1	71.0
Any Ibrutinib (Ibr)-Related TEAE	95.7	97.7	93.0	96.8
Any Grade ≥ 3 Ibrutinib-Related TEAE	57.9	55.8	51.2	61.3
Any Venetoclax (Ven)-Related TEAE	81.1	88.4	76.7	80.6
Any Grade ≥ 3 Venetoclax-Related TEAE	44.5	51.2	34.9	45.2
Any TEAE Leading to Ibr or Ven Discontinuation	15.9	16.3	0	9.7
Any TEAE Leading to Ibr or Ven Discon: Ib Only	10.4	14.0	0	9.7
Any TEAE Leading to Ibr or Ven Discon: Ven Only	1.2	2.3	0	0
Any TEAE Leading to Ibr or Ven Discon: Ibr + Ven	4.3	0	0	0
Any TEAE Leading to Ibr or Ven Dose Reduction	26.2	23.3	25.6	25.8
Any TEAE Leading to Ibr Only Dose Reduction	16.5	16.3	11.6	19.4
Any TEAE Leading to Ven Only Dose Reduction	4.9	2.3	11.6	0
Any TEAE Leading to Both Ibr + Ven Dose Reduction	4.9	4.7	2.3	6.5
Any SAE	34.1	34.9	32.6	41.9
Any Grade ≥ 3 SAE	28.7	32.6	27.9	32.3
Any SAE Related to Ibr or Ven	20.1	18.6	14.0	25.8
Any Ibr-related SAE	17.1	14.0	11.6	22.6
Any Ven-related SAE	6.7	4.7	7.0	12.9
Fatal TEAE	1.2	2.3	0	3.2
Major Hemorrhage TEAE	2.4	2.3	0	3.2
Grade ≥ 3 Major Hemorrhage TEAE	1.8	2.3	0	3.2
Major Hemorrhage SAE	2.4	2.3	0	3.2

End point values	MRD/uMRD Not Confirmed: Open-Label Ibrutinib + Venetoclax			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: percentage of subjects				
number (not applicable)				
Any TEAE	100.0			
Any Grade ≥ 3 TEAE	78.1			
Any Ibrutinib (Ibr)-Related TEAE	93.8			

Any Grade ≥ 3 Ibrutinib-Related TEAE	62.5			
Any Venetoclax (Ven)-Related TEAE	96.9			
Any Grade ≥ 3 Venetoclax-Related TEAE	56.3			
Any TEAE Leading to Ibr or Ven Discontinuation	12.5			
Any TEAE Leading to Ibr or Ven Discon: Ib Only	3.1			
Any TEAE Leading to Ibr or Ven Discon: Ven Only	0			
Any TEAE Leading to Ibr or Ven Discon: Ibr + Ven	9.4			
Any TEAE Leading to Ibr or Ven Dose Reduction	34.4			
Any TEAE Leading to Ibr Only Dose Reduction	25.0			
Any TEAE Leading to Ven Only Dose Reduction	3.1			
Any TEAE Leading to Both Ibr + Ven Dose Reduction	6.3			
Any SAE	37.5			
Any Grade ≥ 3 SAE	28.1			
Any SAE Related to Ibr or Ven	21.9			
Any Ibr-related SAE	18.8			
Any Ven-related SAE	6.3			
Fatal TEAE	0			
Major Hemorrhage TEAE	6.3			
Grade ≥ 3 Major Hemorrhage TEAE	3.1			
Major Hemorrhage SAE	6.3			

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: ORR

End point title	FD Cohort: ORR ^[13]
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End point description:

ORR is defined as the percentage of participants who achieve a best overall response CR, CRi, nPR, PR, or PRL as evaluated by investigator using 2008 IWCLL criteria (Halleck et al.). Participants who did not have any postbaseline response assessment were considered as non-responders. This table is based on response assessments performed on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurs earlier. Kaplan-Meier estimate.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD, for a median follow-up of 69.0 months.

Notes:

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

Justification: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	159	136		
Units: percentage of subjects				
number (confidence interval 95%)	96.2 (93.3 to 99.2)	95.6 (92.1 to 99.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: DOR at 60 Months Landmark Time

End point title	FD Cohort: DOR at 60 Months Landmark Time ^[14]
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End point description:

Duration of response was calculated for participants achieving a response (CR, CRi, nPR, PR) based on 2008 IWCLL response criteria (Halleck et al.) and defined as the interval between the date of initial documentation of a response including PR with lymphocytosis, until disease progression (PD) or death from any cause, whichever occurred first. As the median DOR was not reached as of the median 27.9 months study follow-up, the Kaplan-Meier estimate of DOR at 60 months landmark time was presented.

End point type	Secondary
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End point timeframe:

From initial documentation of a response until PD or death from any cause, whichever occurs first, for a median follow-up of 69.0 months.

Notes:

[14] - 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153 ^[15]	130 ^[16]		
Units: percentage of subjects				
number (confidence interval 95%)	60.5 (52.0 to 68.0)	63.6 (54.4 to 71.4)		

Notes:

[15] - FD Cohort: Participants who achieved PR or better.

[16] - FD Cohort: Participants who achieved PR or better.

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: MRD Negativity Rate

End point title	FD Cohort: MRD Negativity Rate ^[17]
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End point description:

MRD negativity rate is defined as the percentage of participants achieving MRD negativity, which is defined as <1 CLL cell per 10,000 leukocytes ($<1 \times 10^{-4}$) as assessed by flow cytometry of a peripheral blood (PB) or bone marrow (BM) aspirate sample per central laboratory on or prior to initiation of subsequent antineoplastic therapy or, if applicable, reintroduction of study treatment, whichever occurs earlier.

End point type	Secondary
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End point timeframe:

From randomization date until before any subsequent antineoplastic therapy, for a median follow-up of 69.0 months.

Notes:

[17] - 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	159	136		
Units: percentage of subjects				
number (confidence interval 95%)				
BM or PB	78.6 (72.2 to 85.0)	78.7 (71.8 to 85.6)		
BM	59.7 (52.1 to 67.4)	61.8 (53.6 to 69.9)		
PB	76.7 (70.2 to 83.3)	76.5 (69.3 to 83.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: Kaplan-Meier Estimate of PFS Rate at 66 Months Landmark Time

End point title	FD Cohort: Kaplan-Meier Estimate of PFS Rate at 66 Months Landmark Time ^[18]
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End point description:

PFS was defined as time from the first dose date of study treatment until disease progression (PD) or death from any cause, whichever occurs first. Assessment of PD was conducted in accordance with the 2008 IWCLL criteria (Halleck et al). As the median PFS was not reached as of the median 69.0 months study follow-up, the Kaplan-Meier estimate of PFS rate at 66 months landmark time was presented.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to the first confirmed PD or death, for a median follow-up of 69.0 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	159	136		
Units: percentage of subjects				
number (confidence interval 95%)	60.2 (51.7 to 67.7)	63.2 (54.1 to 71.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: Kaplan-Meier Estimate of OS Rate at 66 Months Landmark Time

End point title	FD Cohort: Kaplan-Meier Estimate of OS Rate at 66 Months Landmark Time ^[19]
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End point description:

OS is defined as the time from the first dose date of study treatment until date of death due to any cause. As the median OS was not reached as of the median 69.0 months study follow-up, the Kaplan-Meier estimate of OS rate at 66 months landmark time was presented.

End point type	Secondary
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End point timeframe:

From the first dose of ibrutinib to time of death, for a median follow-up of 69.0 months.

Notes:

[19] - 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated	FD Cohort/Non-Del 17p Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	159	136		
Units: percentage of subjects				
number (confidence interval 95%)	96.1 (91.4 to 98.2)	96.9 (92.1 to 98.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: TLS Risk Reduction Rate With 3-Cycle Ibrutinib Lead-In (Percentage of Participants No Longer High Risk After 3-cycle Lead-in)

End point title	FD Cohort: TLS Risk Reduction Rate With 3-Cycle Ibrutinib Lead-In (Percentage of Participants No Longer High Risk After 3-cycle Lead-in) ^[20]
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End point description:

TLS risk reduction was summarized by the percentage of participants with TLS risk reduced from high at baseline to medium or low after ibrutinib lead-in. A reduction in TLS risk from high risk to medium or low risk is clinically meaningful because there is a reduction in the extent of TLS monitoring and risk of hospitalization. TLS risk category is defined as the tumor burden category, where: Low=All lymph nodes (LN) < 5 cm AND absolute lymphocyte count (ALC) < 25 x 10⁹/L; Medium=Any LN 5 cm to < 10 cm OR ALC ≥ 25 x 10⁹/L; High=Any LN ≥ 10 cm OR ALC ≥ 25 x10⁹/L AND any LN ≥ 5 cm.

End point type	Secondary
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End point timeframe:

Baseline, and last post-baseline value on or prior to venetoclax first dose date (cycle 4 day 1) or, for participants who never received venetoclax, the post-baseline value closest to cycle 4 day 1 (i.e. 84 days after the first dose date of ibrutinib).

Notes:

[20] - 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	34 ^[21]			
Units: percentage of subjects				
number (not applicable)	94.1			

Notes:

[21] - FD Cohort: All Treated Population with baseline TLS high risk

Statistical analyses

No statistical analyses for this end point

Secondary: FD Cohort: Percentage of Participants With TEAEs, Treatment-Emergent SAEs, and Discontinuations Due to TEAEs

End point title	FD Cohort: Percentage of Participants With TEAEs, Treatment-Emergent SAEs, and Discontinuations Due to TEAEs ^[22]
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End point description:

An AE is any untoward medical occurrence, which does not necessarily have a causal relationship with this treatment. An SAE is any untoward medical occurrence that at any dose: results in death; is life-threatening; requires unplanned in-patient hospitalization >24 hours or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event. Severity of events were graded according to the Common Terminology Criteria for Adverse Events version 4.03: mild=grade1, moderate=grade 2, severe=grade 3, life-threatening=grade 4, death=grade 5. Causal relation of study drug and event was assessed as not related, unlikely, possibly or probably related to the study drug.

End point type	Secondary
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End point timeframe:

From first dose until 30 days following last dose of study drug. Overall median treatment duration for the FD cohort was 13.8 months.

Notes:

[22] - 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: Data are summarized for this end point per protocol.

End point values	Fixed Duration (FD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	159			
Units: percentage of subjects				
number (not applicable)				
Any TEAE	99.4			
Any Grade ≥ 3 TEAE	62.3			
Any Ibrutinib (Ibr)-Related TEAE	92.5			
Any Grade ≥ 3 Ibrutinib-Related TEAE	44.7			
Any Venetoclax (Ven)-Related TEAE	84.3			
Any Grade ≥ 3 Venetoclax-Related TEAE	45.3			
Any TEAE Leading to Ibr or Ven Discontinuation	5.0			
Any TEAE Leading to Ibr or Ven Discon: Ibr Only	3.1			
Any TEAE Leading to Ibr or Ven Discon: Ven Only	0			
Any TEAE Leading to Ibr or Ven Discon: Ibr + Ven	1.9			
Any TEAE Leading to Ibr or Ven Dose Reduction	20.8			
Any TEAE Leading to Ibr Only Dose Reduction	5.7			
Any TEAE Leading to Ven Only Dose Reduction	11.3			
Any TEAE Leading to Both Ibr + Ven Dose Reduction	3.8			
Any Grade ≥ 3 SAE	20.1			
Any SAE Related to Ibr or Ven	13.8			
Any Ibr-related SAE	11.9			
Any Ven-related SAE	8.8			
Fatal TEAE	0.6			
Major Hemorrhage TEAE	1.9			
Grade ≥ 3 Major Hemorrhage TEAE	1.3			
Major Hemorrhage SAE	1.3			
Any SAE	23.3			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: Pharmacokinetics (PK) of Ibrutinib When Dosed in Combination With Venetoclax: Observed Maximum Concentration (C_{max})

End point title	MRD Cohort: Pharmacokinetics (PK) of Ibrutinib When Dosed in Combination With Venetoclax: Observed Maximum Concentration (C _{max}) ^[23]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary			
End point timeframe:				
Cycle 6 Day 1: predose, at dose, 1 h (±15 min), 2 h (±15 min), 4 h (±15 min), 6 h (±15 min), 8 h (±15 min)				
Notes:				
[23] - 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: Data are summarized for this end point per protocol.				
End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	130 ^[24]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	88.5 (± 74.3)			

Notes:

[24] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Time to Cmax (Tmax); Time of Last Measurable Concentration (Tlast); Terminal Elimination Half-Life (t1/2,Term)

End point title	MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Time to Cmax (Tmax); Time of Last Measurable Concentration (Tlast); Terminal Elimination Half-Life (t1/2,Term) ^[25]			
End point description:				
MRD Cohort: All treated participants who were evaluable for each PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.				
End point type	Secondary			
End point timeframe:				
Cycle 6 Day 1: predose, at dose, 1 h (±15 min), 2 h (±15 min), 4 h (±15 min), 6 h (±15 min), 8 h (±15 min)				
Notes:				
[25] - 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: Data are summarized for this end point per protocol.				
End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	130 ^[26]			
Units: hours				
median (full range (min-max))				

tmax	2.00 (0.970 to 7.00)			
tlast	24.0 (5.75 to 24.0)			
t1/2term	5.30 (1.47 to 10.5)			

Notes:

[26] - MRD Cohort: All treated participants who were evaluable for each PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Area Under the Plasma Concentration-Time Curve (AUC) Over the Last 24-hour Dosing Interval (AUC0-24h); AUC From Time Zero to the Time of Last Quantifiable Concentration (AUClast)

End point title	MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Area Under the Plasma Concentration-Time Curve (AUC) Over the Last 24-hour Dosing Interval (AUC0-24h); AUC From Time Zero to the Time of Last Quantifiable Concentration (AUClast) ^[27]
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End point description:

MRD Cohort: All treated participants who were evaluable for each PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (±15 min), 2 h (±15 min), 4 h (±15 min), 6 h (±15 min), 8 h (±15 min)

Notes:

[27] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	128 ^[28]			
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h	504 (± 76.3)			
AUClast	480 (± 78.5)			

Notes:

[28] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Ibrutinib When Dosed in Combination With

Venetoclax: Terminal Elimination Rate Constant (λ_z)

End point title	MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Terminal Elimination Rate Constant (λ_z) ^[29]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (± 15 min), 2 h (± 15 min), 4 h (± 15 min), 6 h (± 15 min), 8 h (± 15 min)

Notes:

[29] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	91 ^[30]			
Units: 1/h				
geometric mean (geometric coefficient of variation)	0.132 (± 44.5)			

Notes:

[30] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Apparent Total Clearance at Steady-State (CL_{ss}/F)

End point title	MRD Cohort: PK of Ibrutinib When Dosed in Combination With Venetoclax: Apparent Total Clearance at Steady-State (CL_{ss}/F) ^[31]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (± 15 min), 2 h (± 15 min), 4 h (± 15 min), 6 h (± 15 min), 8 h (± 15 min)

Notes:

[31] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	128 ^[32]			
Units: L/h				
geometric mean (geometric coefficient of variation)	833 (\pm 90.9)			

Notes:

[32] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: Cmax

End point title	MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: Cmax ^[33]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (\pm 15 min), 2 h (\pm 15 min), 4 h (\pm 15 min), 6 h (\pm 15 min), 8 h (\pm 15 min)

Notes:

[33] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	131 ^[34]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3034 (\pm 56.3)			

Notes:

[34] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: Tmax

End point title	MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: Tmax ^[35]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (± 15 min), 2 h (± 15 min), 4 h (± 15 min), 6 h (± 15 min), 8 h (± 15 min)

Notes:

[35] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	131 ^[36]			
Units: hours				
median (full range (min-max))	6.00 (0.00 to 8.08)			

Notes:

[36] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: AUC0-24h

End point title	MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: AUC0-24h ^[37]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (± 15 min), 2 h (± 15 min), 4 h (± 15 min), 6 h (± 15 min), 8 h (± 15 min)

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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	131 ^[38]			
Units: ng*h/mL				

geometric mean (geometric coefficient of variation)	48993 (\pm 66.2)			
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Notes:

[38] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: CLss/F

End point title	MRD Cohort: PK of Venetoclax When Dosed in Combination With Ibrutinib: CLss/F ^[39]
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End point description:

MRD Cohort: All treated participants who were evaluable for PK analysis. Data were collected for the MRD cohort only, and without regard to uMRD confirmation status/randomization group, as pre-specified for this analysis.

End point type	Secondary
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End point timeframe:

Cycle 6 Day 1: predose, at dose, 1 h (\pm 15 min), 2 h (\pm 15 min), 4 h (\pm 15 min), 6 h (\pm 15 min), 8 h (\pm 15 min)

Notes:

[39] - 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: Data are summarized for this end point per protocol.

End point values	Minimal Residual Disease (MRD) Cohort: All Treated			
Subject group type	Reporting group			
Number of subjects analysed	131 ^[40]			
Units: L/h				
geometric mean (geometric coefficient of variation)	8.16 (\pm 69.7)			

Notes:

[40] - MRD Cohort: All treated participants who were evaluable for PK analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose until 30 days following last dose of study drug. Overall median treatment duration was 45.1 months for the MRD cohort and 13.8 months for the FD cohort.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	MRD Cohort: Pre-Dose
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Reporting group description:

All reported AEs started prior to the first dose date of any study treatment in the MRD Cohort.

Reporting group title	FD Cohort: Pre-Dose
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Reporting group description:

All reported AEs that started prior to the first dose date of any study treatment in the FD Cohort.

Reporting group title	FD Cohort: All Subjects
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Reporting group description:

Subjects in the FD Cohort received 420mg of single agent ibrutinib for first 3 cycles followed by ibrutinib plus venetoclax combination treatment (ibrutinib 420mg and venetoclax 400mg orally once daily on a continuous schedule) for 12 cycles (1 cycle = 28 days) or until PD or unacceptable toxicity.

1. For subjects who did not receive any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course.
2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	MRD Cohort: Confirmed uMRD (IbrVen->Ibr)
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Reporting group description:

Subjects in the MRD Cohort with confirmed uMRD received 420mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (1 cycle = 28 days) prior to randomization (prerandomization phase). Subjects with confirmed uMRD were randomized to receive ibrutinib 420mg orally once daily on a continuous schedule until MRD-positive relapse, clinical PD, or unacceptable toxicity.

1. For subjects who did not receive any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course.
2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	MRD Cohort: All Subjects
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Reporting group description:

Subjects in the MRD Cohort received 420mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (1 cycle = 28 days) prior to randomization (pre-randomization phase). Subjects with confirmed uMRD were randomized to blinded ibrutinib 420mg or placebo orally once daily on a continuous schedule until PD or unacceptable toxicity. Subjects with uMRD not confirmed were randomized to open-label ibrutinib 420mg or open-label ibrutinib 420mg plus venetoclax 400mg orally once daily on a continuous schedule until PD or unacceptable toxicity. 1. For subjects who did not receive reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course. 2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	MRD Cohort: Confirmed uMRD (IbrVen->Pbo)
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Reporting group description:

Subjects in the MRD Cohort with confirmed uMRD received 420mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (1 cycle = 28 days) prior to randomization (pre-randomization phase). Subjects with confirmed uMRD were randomized to receive placebo orally once daily on a continuous schedule until MRD-positive relapse, clinical PD or unacceptable toxicity.

1. For subjects who did not receive any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course.

2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	MRD Cohort: uMRD Not Confirmed (IbrVen->Ibr)
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Reporting group description:

Subjects in the MRD Cohort with uMRD not confirmed received 420mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (1 cycle = 28 days) prior to randomization (pre-randomization phase). Subjects with uMRD not confirmed were randomized to receive open-label ibrutinib 420 mg orally once daily on a continuous schedule until PD or unacceptable toxicity.

1. For subjects who did not receive any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course.
2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	MRD Cohort: uMRD Not Confirmed (IbrVen->IbrVen)
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Reporting group description:

Subjects in the MRD Cohort with uMRD not confirmed received 420mg of single-agent ibrutinib for the first 3 cycles followed by ibrutinib plus venetoclax combination treatment for at least 12 cycles (1 cycle = 28 days) prior to randomization (pre-randomization phase). Subjects with uMRD not confirmed were randomized to receive open-label ibrutinib 420 mg and venetoclax 400 mg orally once daily on a continuous schedule until PD or unacceptable toxicity.

1. For subjects who did not receive any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment over the whole study course.
2. For subjects who received any reintroduced treatment, includes all reported AEs started after the first dose date of the first-line treatment and prior to the first dose date of the reintroduced treatment.

Reporting group title	FD Cohort: Reintroduced Ibrutinib
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Reporting group description:

All reported AEs in the FD Cohort that started after the first dose date of reintroduced treatment with ibrutinib.

Reporting group title	FD Cohort: Reintroduced Ibr+Ven
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Reporting group description:

All reported AEs in the FD Cohort that started after the first dose date of reintroduced treatment with ibrutinib + venetoclax.

Reporting group title	MRD Cohort: Reintroduced Ibrutinib
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Reporting group description:

All reported AEs in the MRD Cohort that started after the first dose date of reintroduced treatment with ibrutinib.

Reporting group title	MRD Cohort: Reintroduced Ven + Continued Ibr
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Reporting group description:

All reported AEs in the MRD Cohort that started after the first dose date of reintroduced treatment with venetoclax and continued ibrutinib.

Serious adverse events	MRD Cohort: Pre-Dose	FD Cohort: Pre-Dose	FD Cohort: All Subjects
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 164 (1.22%)	1 / 159 (0.63%)	37 / 159 (23.27%)
number of deaths (all causes)	0	0	5
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSITIONAL CELL CARCINOMA			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 ONCOCYTOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
SUDDEN CARDIAC DEATH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PYREXIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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			
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC HAEMATOMA			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	0 / 159 (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
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
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 DISTRESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER WITH MIXED ANXIETY AND DEPRESSED MOOD			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

BLOOD PRESSURE DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA B VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
MALFORMATION VENOUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DILATED CARDIOMYOPATHY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYARRHYTHMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL VENOUS SINUS THROMBOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VESTIBULAR MIGRAINE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYSIS			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
EYE HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MACULAR OEDEMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL SPASM			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETROPERITONEAL HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGITIS ACUTE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
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 ACUTE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ARTHRALGIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL SYNOVIAL CYST			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOPOROSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 INFECTIVE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICEAL ABSCESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 ORBITAL			
subjects affected / exposed	1 / 164 (0.61%)	0 / 159 (0.00%)	0 / 159 (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
COVID-19			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 PNEUMONIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER DISSEMINATED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS BACTERIAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PILONIDAL DISEASE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 LEGIONELLA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYOMYOSITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS			
subjects affected / exposed	1 / 164 (0.61%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
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 INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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 UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WEST NILE VIRAL INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
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			
HYPONATRAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MRD Cohort: Confirmed uMRD (IbrVen->Ibr)	MRD Cohort: All Subjects	MRD Cohort: Confirmed uMRD (IbrVen->Pbo)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 43 (34.88%)	63 / 164 (38.41%)	14 / 43 (32.56%)
number of deaths (all causes)	1	3	0
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			

subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
RENAL CANCER			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL ONCOCYTOMA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PAIN			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 CARDIAC DEATH			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PYREXIA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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			
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC HAEMATOMA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			

subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	1 / 43 (2.33%)	2 / 164 (1.22%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSпноEA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER WITH MIXED ANXIETY AND DEPRESSED			

MOOD			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
SCHIZOPHRENIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD PRESSURE DECREASED			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA B VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Congenital, familial and genetic disorders			
MALFORMATION VENOUS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	2 / 2	7 / 7	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
CARDIAC ARREST			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
DILATED CARDIOMYOPATHY			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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

MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
PERICARDITIS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 TACHYARRHYTHMIA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
EPILEPSY			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 VENOUS SINUS THROMBOSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 43 (2.33%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VESTIBULAR MIGRAINE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (0.00%)	4 / 164 (2.44%)	3 / 43 (6.98%)
occurrences causally related to treatment / all	0 / 0	3 / 4	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
EYE HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
MACULAR OEDEMA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RETINAL HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (0.00%)	2 / 164 (1.22%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
COLITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
OESOPHAGEAL SPASM			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STONE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 ACUTE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
ARTHRALGIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
SPINAL SYNOVIAL CYST			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOPOROSIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	1 / 43 (2.33%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS INFECTIVE			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

APPENDICITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
APPENDICEAL ABSCESS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAMPYLOBACTER INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS ORBITAL			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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 / 43 (0.00%)	2 / 164 (1.22%)	2 / 43 (4.65%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			

subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
HERPES ZOSTER DISSEMINATED			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
INFLUENZA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS BACTERIAL			

subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PILONIDAL DISEASE			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
PNEUMONIA			
subjects affected / exposed	3 / 43 (6.98%)	9 / 164 (5.49%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	1 / 3	4 / 9	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA LEGIONELLA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYOMYOSITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS			

subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (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
WEST NILE VIRAL INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPONATRAEMIA			

subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
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	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MRD Cohort: uMRD Not Confirmed (IbrVen->Ibr)	MRD Cohort: uMRD Not Confirmed (IbrVen->IbrVen)	FD Cohort: Reintroduced Ibrutinib
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 31 (41.94%)	12 / 32 (37.50%)	6 / 18 (33.33%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
RENAL CANCER			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 ONCOCYTOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 CARDIAC DEATH			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			
HEAVY MENSTRUAL BLEEDING			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC HAEMATOMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER WITH MIXED ANXIETY AND DEPRESSED MOOD			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
SCHIZOPHRENIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD PRESSURE DECREASED			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA B VIRUS TEST POSITIVE			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
Injury, poisoning and procedural complications			
FEMUR FRACTURE			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
MALFORMATION VENOUS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CARDIAC FAILURE			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DILATED CARDIOMYOPATHY			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 TACHYARRHYTHMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			

ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 VENOUS SINUS THROMBOSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			

subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (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
VESTIBULAR MIGRAINE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYSIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO POSITIONAL			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
EYE HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
MACULAR OEDEMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
DIARRHOEA			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
COLITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL SPASM			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STONE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 ACUTE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
ARTHRALGIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
SPINAL SYNOVIAL CYST			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

OSTEOPOROSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICEAL ABSCESS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 ORBITAL			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 PNEUMONIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER DISSEMINATED			

subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
INFLUENZA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (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
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS BACTERIAL			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PILONIDAL DISEASE			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	3 / 31 (9.68%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 LEGIONELLA			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYOMYOSITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (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
WEST NILE VIRAL INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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			
HYPONATRAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
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 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	FD Cohort: Reintroduced Ibr+Ven	MRD Cohort: Reintroduced Ibrutinib	MRD Cohort: Reintroduced Ven + Continued Ibr
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL ADENOCARCINOMA			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSITIONAL CELL CARCINOMA			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 ONCOCYTOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 CARDIAC DEATH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PYREXIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY POSITIVE VASCULITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC HAEMATOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER WITH MIXED ANXIETY AND DEPRESSED MOOD			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

BLOOD PRESSURE DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA B VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
MALFORMATION VENOUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DILATED CARDIOMYOPATHY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 TACHYARRHYTHMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 VENOUS SINUS THROMBOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VESTIBULAR MIGRAINE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOLYSIS			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
EYE HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MACULAR OEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL SPASM			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 ACUTE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ARTHRALGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL SYNOVIAL CYST			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOPOROSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 INFECTIVE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICEAL ABSCESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (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
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 ORBITAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 PNEUMONIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER DISSEMINATED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS BACTERIAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PILONIDAL DISEASE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 LEGIONELLA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYOMYOSITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WEST NILE VIRAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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			
HYPONATRAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
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 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MRD Cohort: Pre-Dose	FD Cohort: Pre-Dose	FD Cohort: All Subjects
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 164 (0.61%)	1 / 159 (0.63%)	156 / 159 (98.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	4
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	24 / 159 (15.09%)
occurrences (all)	0	0	33
PHLEBITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	9 / 159 (5.66%)
occurrences (all)	0	0	13
CHEST PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
CHEST DISCOMFORT			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
CHILLS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	5

INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	7
FATIGUE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	39 / 159 (24.53%)
occurrences (all)	0	0	51
MALAISE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	7
INJECTION SITE BRUISING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	11 / 159 (6.92%)
occurrences (all)	0	0	12
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	11 / 159 (6.92%)
occurrences (all)	0	0	11
PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	7
PYREXIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	22 / 159 (13.84%)
occurrences (all)	0	0	35
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
ERECTILE DYSFUNCTION			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
TESTICULAR SWELLING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	28 / 159 (17.61%)
occurrences (all)	0	0	34
DYSPNOEA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	11 / 159 (6.92%)
occurrences (all)	0	0	11
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
EPISTAXIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	19 / 159 (11.95%)
occurrences (all)	0	0	27
HAEMOPTYSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	4
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	17 / 159 (10.69%)
occurrences (all)	0	0	19
NASAL DRYNESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
NASAL CONGESTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
SINUS CONGESTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
DEPRESSION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
CONFUSIONAL STATE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
AGITATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	8
BLOOD BILIRUBIN INCREASED			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	15
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	9 / 159 (5.66%)
occurrences (all)	0	0	16
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
WEIGHT DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	8 / 159 (5.03%)
occurrences (all)	0	0	14
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	16 / 159 (10.06%)
occurrences (all)	0	0	38
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	18
Injury, poisoning and procedural complications			
ARTHROPOD BITE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	5
HAND FRACTURE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
FALL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
EYE CONTUSION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	24 / 159 (15.09%)
occurrences (all)	0	0	25
LIMB INJURY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
RIB FRACTURE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
SCRATCH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
SKIN ABRASION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
SKIN LACERATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
WOUND HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	7

PALPITATIONS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	15 / 159 (9.43%)
occurrences (all)	0	0	17
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	4
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Nervous system disorders			
BRAIN FOG			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
HYPOAESTHESIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	39 / 159 (24.53%)
occurrences (all)	0	0	55
DYSGEUSIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
DIZZINESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	27 / 159 (16.98%)
occurrences (all)	0	0	34
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
PARAESTHESIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
SCIATICA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
TREMOR			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	35 / 159 (22.01%)
occurrences (all)	0	0	44
ANAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	10 / 159 (6.29%)
occurrences (all)	0	2	17
LYMPHOCYTOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
NEUTROPENIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	65 / 159 (40.88%)
occurrences (all)	0	0	169
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	4
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	21 / 159 (13.21%)
occurrences (all)	0	0	38

Ear and labyrinth disorders DEAFNESS NEUROSENSORY subjects affected / exposed occurrences (all) VERTIGO subjects affected / exposed occurrences (all)	0 / 164 (0.00%) 0 0 / 164 (0.00%) 0	0 / 159 (0.00%) 0 0 / 159 (0.00%) 0	0 / 159 (0.00%) 0 4 / 159 (2.52%) 4
Eye disorders CONJUNCTIVAL HYPERAEMIA subjects affected / exposed occurrences (all) CATARACT subjects affected / exposed occurrences (all) RETINAL DETACHMENT subjects affected / exposed occurrences (all) DRY EYE subjects affected / exposed occurrences (all) RETINAL TEAR subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) UVEITIS subjects affected / exposed occurrences (all) VITREOUS HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0	0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 0 / 159 (0.00%) 0	0 / 159 (0.00%) 0 1 / 159 (0.63%) 1 0 / 159 (0.00%) 0 3 / 159 (1.89%) 3 1 / 159 (0.63%) 1 2 / 159 (1.26%) 2 0 / 159 (0.00%) 0 1 / 159 (0.63%) 1
Gastrointestinal disorders ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all) ABDOMINAL DISTENSION	0 / 164 (0.00%) 0 	0 / 159 (0.00%) 0 	4 / 159 (2.52%) 5

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	10 / 159 (6.29%)
occurrences (all)	0	0	11
ABDOMINAL PAIN			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	13 / 159 (8.18%)
occurrences (all)	0	1	16
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	14 / 159 (8.81%)
occurrences (all)	0	0	15
APHTHOUS ULCER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	8 / 159 (5.03%)
occurrences (all)	0	0	10
COLITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	25 / 159 (15.72%)
occurrences (all)	0	1	31
DRY MOUTH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
DIARRHOEA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	99 / 159 (62.26%)
occurrences (all)	0	0	203
DYSPEPSIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	29 / 159 (18.24%)
occurrences (all)	0	0	38
FLATULENCE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
DYSPHAGIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
GASTRITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
HAEMORRHOIDAL HAEMORRHAGE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
GLOSSODYNIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	16 / 159 (10.06%)
occurrences (all)	0	1	19
HAEMORRHOIDS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	2
INGUINAL HERNIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
LIP BLISTER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
MOUTH ULCERATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	24 / 159 (15.09%)
occurrences (all)	0	0	30
ORAL PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
NAUSEA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	68 / 159 (42.77%)
occurrences (all)	0	0	97
PROCTALGIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0

SALIVARY GLAND ENLARGEMENT			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
STOMATITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	21 / 159 (13.21%)
occurrences (all)	0	0	33
VOMITING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	33 / 159 (20.75%)
occurrences (all)	0	0	48
TOOTHACHE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
BLISTER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	4
ALOPECIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	6
ACNE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
BLOOD BLISTER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	7
DERMATITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
DERMATITIS ACNEIFORM			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	16 / 159 (10.06%)
occurrences (all)	0	0	18
ECCHYMOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
ECZEMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
ERYTHEMA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	8 / 159 (5.03%)
occurrences (all)	0	0	8
HYPERHIDROSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	6
NIGHT SWEATS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	5
NAIL RIDGING			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
HYPERKERATOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
ONYCHOCLASIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	14 / 159 (8.81%)
occurrences (all)	0	0	14
PRURITUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	17 / 159 (10.69%)
occurrences (all)	0	0	19
PETECHIAE			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	17 / 159 (10.69%)
occurrences (all)	0	0	23
PSORIASIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
RASH			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	10 / 159 (6.29%)
occurrences (all)	0	0	12
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	9 / 159 (5.66%)
occurrences (all)	0	0	11
RASH MACULAR			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	27 / 159 (16.98%)
occurrences (all)	0	0	32
SKIN ATROPHY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
SKIN FISSURES			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	6
SKIN FRAGILITY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
SKIN LESION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	8 / 159 (5.03%)
occurrences (all)	0	0	8
SKIN MASS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Renal and urinary disorders			

HAEMATURIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	9 / 159 (5.66%)
occurrences (all)	0	0	9
NEPHROLITHIASIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
POLLAKIURIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
JOINT STIFFNESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
FOOT DEFORMITY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
BONE PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
BACK PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	20 / 159 (12.58%)
occurrences (all)	0	0	22
ARTHRALGIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	52 / 159 (32.70%)
occurrences (all)	0	0	84
OSTEOARTHRITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
NECK PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	7
MYALGIA			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	23 / 159 (14.47%)
occurrences (all)	0	0	30
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	21 / 159 (13.21%)
occurrences (all)	0	0	25
MUSCLE SPASMS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	47 / 159 (29.56%)
occurrences (all)	0	0	66
PERIARTHRITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
SPINAL PAIN			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	6
CELLULITIS			
subjects affected / exposed	1 / 164 (0.61%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	1	0	7
CAMPYLOBACTER GASTROENTERITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	6
EYE INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
FOLLICULITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3

FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
COVID-19			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	8 / 159 (5.03%)
occurrences (all)	0	0	9
CYSTITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
FURUNCLE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	6 / 159 (3.77%)
occurrences (all)	0	0	7
INFLUENZA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	10 / 159 (6.29%)
occurrences (all)	0	0	10
INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	3
LOCALISED INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	8
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	4
NASOPHARYNGITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	12 / 159 (7.55%)
occurrences (all)	0	0	16
NOROVIRUS INFECTION			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
ORAL HERPES			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	8
OTITIS MEDIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
PHARYNGITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
PARONYCHIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	5
PNEUMONIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	5
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
PROSTATIC ABSCESS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
SIALOADENITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
TINEA PEDIS			

subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
SKIN INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	4 / 159 (2.52%)
occurrences (all)	0	0	4
SINUSITIS			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	10 / 159 (6.29%)
occurrences (all)	0	0	17
TOOTH INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	39 / 159 (24.53%)
occurrences (all)	0	0	50
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	12 / 159 (7.55%)
occurrences (all)	0	0	17
VIRAL INFECTION			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	9
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	3 / 159 (1.89%)
occurrences (all)	0	0	3
HYPERGLYCAEMIA			

subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	6 / 159 (3.77%)
occurrences (all)	0	1	7
HYPERKALAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	1 / 159 (0.63%)	5 / 159 (3.14%)
occurrences (all)	0	1	5
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	9
HYPERURICAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	12 / 159 (7.55%)
occurrences (all)	0	0	21
HYPOCALCAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1
HYPOKALAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	8
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	8
HYPONATRAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	7 / 159 (4.40%)
occurrences (all)	0	0	12
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	5 / 159 (3.14%)
occurrences (all)	0	0	6
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 164 (0.00%)	0 / 159 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	0	1

Non-serious adverse events	MRD Cohort: Confirmed uMRD (IbrVen->Ibr)	MRD Cohort: All Subjects	MRD Cohort: Confirmed uMRD (IbrVen->Pbo)
Total subjects affected by non-serious adverse events subjects affected / exposed	43 / 43 (100.00%)	163 / 164 (99.39%)	43 / 43 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) SQUAMOUS CELL CARCINOMA subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 3	2 / 164 (1.22%) 3	0 / 43 (0.00%) 0
MELANOCYTIC NAEVUS subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	2 / 164 (1.22%) 2	1 / 43 (2.33%) 1
BASAL CELL CARCINOMA subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 6	12 / 164 (7.32%) 18	5 / 43 (11.63%) 5
Vascular disorders HYPERTENSION subjects affected / exposed occurrences (all)	15 / 43 (34.88%) 26	45 / 164 (27.44%) 68	11 / 43 (25.58%) 16
PHLEBITIS subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	2 / 164 (1.22%) 2	0 / 43 (0.00%) 0
General disorders and administration site conditions ASTHENIA subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	12 / 164 (7.32%) 15	3 / 43 (6.98%) 4
CHEST PAIN subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	6 / 164 (3.66%) 6	1 / 43 (2.33%) 1
CHEST DISCOMFORT subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	7 / 164 (4.27%) 8	2 / 43 (4.65%) 2
CHILLS subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 5	14 / 164 (8.54%) 19	5 / 43 (11.63%) 6
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	4 / 43 (9.30%)	11 / 164 (6.71%)	1 / 43 (2.33%)
occurrences (all)	5	12	1
FATIGUE			
subjects affected / exposed	14 / 43 (32.56%)	56 / 164 (34.15%)	21 / 43 (48.84%)
occurrences (all)	25	102	37
MALAISE			
subjects affected / exposed	1 / 43 (2.33%)	6 / 164 (3.66%)	3 / 43 (6.98%)
occurrences (all)	2	7	3
INJECTION SITE BRUISING			
subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	1 / 43 (2.33%)
occurrences (all)	2	5	1
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	5	0
OEDEMA PERIPHERAL			
subjects affected / exposed	8 / 43 (18.60%)	22 / 164 (13.41%)	6 / 43 (13.95%)
occurrences (all)	11	34	11
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 43 (0.00%)	6 / 164 (3.66%)	2 / 43 (4.65%)
occurrences (all)	0	6	2
PAIN			
subjects affected / exposed	0 / 43 (0.00%)	9 / 164 (5.49%)	2 / 43 (4.65%)
occurrences (all)	0	10	2
PYREXIA			
subjects affected / exposed	10 / 43 (23.26%)	31 / 164 (18.90%)	4 / 43 (9.30%)
occurrences (all)	12	44	7
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	1 / 43 (2.33%)	7 / 164 (4.27%)	2 / 43 (4.65%)
occurrences (all)	1	7	2
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
ERECTILE DYSFUNCTION			

subjects affected / exposed	3 / 43 (6.98%)	7 / 164 (4.27%)	0 / 43 (0.00%)
occurrences (all)	3	7	0
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
TESTICULAR SWELLING			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	3 / 43 (6.98%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	4	4	0
COUGH			
subjects affected / exposed	15 / 43 (34.88%)	46 / 164 (28.05%)	17 / 43 (39.53%)
occurrences (all)	20	63	25
DYSPNOEA			
subjects affected / exposed	11 / 43 (25.58%)	22 / 164 (13.41%)	6 / 43 (13.95%)
occurrences (all)	12	25	6
DYSPNOEA EXERTIONAL			
subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	3 / 43 (6.98%)
occurrences (all)	2	5	3
EPISTAXIS			
subjects affected / exposed	10 / 43 (23.26%)	30 / 164 (18.29%)	8 / 43 (18.60%)
occurrences (all)	18	51	17
HAEMOPTYSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 43 (4.65%)	6 / 164 (3.66%)	1 / 43 (2.33%)
occurrences (all)	2	6	1
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 43 (2.33%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
PRODUCTIVE COUGH			

subjects affected / exposed	5 / 43 (11.63%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	5	7	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	10 / 43 (23.26%)	39 / 164 (23.78%)	9 / 43 (20.93%)
occurrences (all)	16	63	15
NASAL DRYNESS			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	3 / 43 (6.98%)
occurrences (all)	1	5	3
NASAL CONGESTION			
subjects affected / exposed	7 / 43 (16.28%)	18 / 164 (10.98%)	4 / 43 (9.30%)
occurrences (all)	8	21	5
SINUS CONGESTION			
subjects affected / exposed	5 / 43 (11.63%)	10 / 164 (6.10%)	2 / 43 (4.65%)
occurrences (all)	5	10	2
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	3 / 43 (6.98%)	21 / 164 (12.80%)	6 / 43 (13.95%)
occurrences (all)	3	22	7
DEPRESSION			
subjects affected / exposed	4 / 43 (9.30%)	8 / 164 (4.88%)	0 / 43 (0.00%)
occurrences (all)	4	9	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
ANXIETY			
subjects affected / exposed	4 / 43 (9.30%)	13 / 164 (7.93%)	2 / 43 (4.65%)
occurrences (all)	4	14	3
AGITATION			
subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	5	0
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	5 / 43 (11.63%)	16 / 164 (9.76%)	4 / 43 (9.30%)
occurrences (all)	6	20	4
BLOOD BILIRUBIN INCREASED			

subjects affected / exposed	1 / 43 (2.33%)	7 / 164 (4.27%)	0 / 43 (0.00%)
occurrences (all)	1	20	0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 43 (9.30%)	17 / 164 (10.37%)	5 / 43 (11.63%)
occurrences (all)	7	33	6
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	5 / 43 (11.63%)	17 / 164 (10.37%)	5 / 43 (11.63%)
occurrences (all)	5	24	6
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	3 / 43 (6.98%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	4	4	0
WEIGHT DECREASED			
subjects affected / exposed	5 / 43 (11.63%)	8 / 164 (4.88%)	2 / 43 (4.65%)
occurrences (all)	5	8	2
PLATELET COUNT DECREASED			
subjects affected / exposed	5 / 43 (11.63%)	9 / 164 (5.49%)	2 / 43 (4.65%)
occurrences (all)	8	12	2
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	2 / 43 (4.65%)
occurrences (all)	2	6	2
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	2 / 43 (4.65%)
occurrences (all)	0	2	2
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	6	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			

subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	5	0
HAND FRACTURE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	5 / 43 (11.63%)	10 / 164 (6.10%)	2 / 43 (4.65%)
occurrences (all)	6	11	2
EYE CONTUSION			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
CONTUSION			
subjects affected / exposed	10 / 43 (23.26%)	40 / 164 (24.39%)	12 / 43 (27.91%)
occurrences (all)	14	63	20
LIMB INJURY			
subjects affected / exposed	1 / 43 (2.33%)	6 / 164 (3.66%)	3 / 43 (6.98%)
occurrences (all)	1	6	3
RIB FRACTURE			
subjects affected / exposed	1 / 43 (2.33%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	1	3	0
SCRATCH			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
SKIN ABRASION			
subjects affected / exposed	1 / 43 (2.33%)	9 / 164 (5.49%)	1 / 43 (2.33%)
occurrences (all)	1	10	1
SKIN LACERATION			
subjects affected / exposed	3 / 43 (6.98%)	9 / 164 (5.49%)	2 / 43 (4.65%)
occurrences (all)	3	9	2
WOUND HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 43 (4.65%)	13 / 164 (7.93%)	3 / 43 (6.98%)
occurrences (all)	2	18	3

PALPITATIONS			
subjects affected / exposed	11 / 43 (25.58%)	27 / 164 (16.46%)	8 / 43 (18.60%)
occurrences (all)	18	39	11
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	2 / 43 (4.65%)
occurrences (all)	0	4	2
SINUS BRADYCARDIA			
subjects affected / exposed	2 / 43 (4.65%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	6	6	0
Nervous system disorders			
BRAIN FOG			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA			
subjects affected / exposed	3 / 43 (6.98%)	12 / 164 (7.32%)	4 / 43 (9.30%)
occurrences (all)	3	15	5
HEADACHE			
subjects affected / exposed	15 / 43 (34.88%)	52 / 164 (31.71%)	18 / 43 (41.86%)
occurrences (all)	27	92	32
DYSGEUSIA			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	2 / 43 (4.65%)
occurrences (all)	1	6	3
DIZZINESS			
subjects affected / exposed	10 / 43 (23.26%)	32 / 164 (19.51%)	9 / 43 (20.93%)
occurrences (all)	14	45	11
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
MEMORY IMPAIRMENT			
subjects affected / exposed	3 / 43 (6.98%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	4	5	0
PARAESTHESIA			
subjects affected / exposed	4 / 43 (9.30%)	14 / 164 (8.54%)	4 / 43 (9.30%)
occurrences (all)	4	18	6
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	3 / 43 (6.98%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	4	5	0
SCIATICA			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	1 / 43 (2.33%)
occurrences (all)	1	5	1
SYNCOPE			
subjects affected / exposed	2 / 43 (4.65%)	7 / 164 (4.27%)	0 / 43 (0.00%)
occurrences (all)	2	7	0
TREMOR			
subjects affected / exposed	3 / 43 (6.98%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	5	5	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	2 / 43 (4.65%)
occurrences (all)	0	4	2
Blood and lymphatic system disorders			
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	12 / 43 (27.91%)	41 / 164 (25.00%)	7 / 43 (16.28%)
occurrences (all)	19	62	9
ANAEMIA			
subjects affected / exposed	5 / 43 (11.63%)	14 / 164 (8.54%)	0 / 43 (0.00%)
occurrences (all)	10	26	0
LYMPHOCYTOSIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	2 / 43 (4.65%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	3	3	0
NEUTROPENIA			
subjects affected / exposed	24 / 43 (55.81%)	71 / 164 (43.29%)	15 / 43 (34.88%)
occurrences (all)	107	246	36
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	3	13	0
THROMBOCYTOPENIA			
subjects affected / exposed	9 / 43 (20.93%)	33 / 164 (20.12%)	5 / 43 (11.63%)
occurrences (all)	21	72	9

Ear and labyrinth disorders DEAFNESS NEUROSENSORY subjects affected / exposed occurrences (all) VERTIGO subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0 2 / 43 (4.65%) 2	1 / 164 (0.61%) 1 9 / 164 (5.49%) 12	0 / 43 (0.00%) 0 2 / 43 (4.65%) 4
Eye disorders CONJUNCTIVAL HYPERAEMIA subjects affected / exposed occurrences (all) CATARACT subjects affected / exposed occurrences (all) RETINAL DETACHMENT subjects affected / exposed occurrences (all) DRY EYE subjects affected / exposed occurrences (all) RETINAL TEAR subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) UVEITIS subjects affected / exposed occurrences (all) VITREOUS HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0 2 / 43 (4.65%) 2 0 / 43 (0.00%) 0 2 / 43 (4.65%) 2 0 / 43 (0.00%) 0 4 / 43 (9.30%) 6 0 / 43 (0.00%) 0 0 / 43 (0.00%) 0	0 / 164 (0.00%) 0 5 / 164 (3.05%) 6 1 / 164 (0.61%) 1 8 / 164 (4.88%) 8 1 / 164 (0.61%) 1 13 / 164 (7.93%) 15 0 / 164 (0.00%) 0 0 / 164 (0.00%) 0	0 / 43 (0.00%) 0 2 / 43 (4.65%) 3 0 / 43 (0.00%) 0 2 / 43 (4.65%) 2 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0 0 / 43 (0.00%) 0
Gastrointestinal disorders ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all) ABDOMINAL DISTENSION	5 / 43 (11.63%) 5	10 / 164 (6.10%) 12	1 / 43 (2.33%) 1

subjects affected / exposed	4 / 43 (9.30%)	15 / 164 (9.15%)	5 / 43 (11.63%)
occurrences (all)	6	21	9
ABDOMINAL PAIN			
subjects affected / exposed	8 / 43 (18.60%)	28 / 164 (17.07%)	10 / 43 (23.26%)
occurrences (all)	9	34	11
ABDOMINAL PAIN UPPER			
subjects affected / exposed	7 / 43 (16.28%)	25 / 164 (15.24%)	5 / 43 (11.63%)
occurrences (all)	9	34	6
APHTHOUS ULCER			
subjects affected / exposed	1 / 43 (2.33%)	7 / 164 (4.27%)	5 / 43 (11.63%)
occurrences (all)	1	10	8
COLITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	11 / 43 (25.58%)	34 / 164 (20.73%)	8 / 43 (18.60%)
occurrences (all)	14	47	11
DRY MOUTH			
subjects affected / exposed	4 / 43 (9.30%)	8 / 164 (4.88%)	2 / 43 (4.65%)
occurrences (all)	4	8	2
DIARRHOEA			
subjects affected / exposed	34 / 43 (79.07%)	119 / 164 (72.56%)	28 / 43 (65.12%)
occurrences (all)	91	435	72
DYSPEPSIA			
subjects affected / exposed	10 / 43 (23.26%)	30 / 164 (18.29%)	5 / 43 (11.63%)
occurrences (all)	11	40	9
FLATULENCE			
subjects affected / exposed	1 / 43 (2.33%)	9 / 164 (5.49%)	3 / 43 (6.98%)
occurrences (all)	1	9	3
DYSPHAGIA			
subjects affected / exposed	1 / 43 (2.33%)	3 / 164 (1.83%)	1 / 43 (2.33%)
occurrences (all)	1	4	1
GASTRITIS			
subjects affected / exposed	4 / 43 (9.30%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	4	7	1
HAEMORRHOIDAL HAEMORRHAGE			

subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	1 / 43 (2.33%)
occurrences (all)	2	5	1
GLOSSODYNIA			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
GINGIVAL BLEEDING			
subjects affected / exposed	2 / 43 (4.65%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	2	8	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	10 / 43 (23.26%)	30 / 164 (18.29%)	4 / 43 (9.30%)
occurrences (all)	11	36	6
HAEMORRHOIDS			
subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	3 / 43 (6.98%)
occurrences (all)	1	4	3
INGUINAL HERNIA			
subjects affected / exposed	2 / 43 (4.65%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	2	2	0
LIP BLISTER			
subjects affected / exposed	1 / 43 (2.33%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
MOUTH ULCERATION			
subjects affected / exposed	6 / 43 (13.95%)	19 / 164 (11.59%)	4 / 43 (9.30%)
occurrences (all)	8	31	4
ORAL PAIN			
subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	1 / 43 (2.33%)
occurrences (all)	1	4	1
NAUSEA			
subjects affected / exposed	21 / 43 (48.84%)	80 / 164 (48.78%)	20 / 43 (46.51%)
occurrences (all)	40	136	29
PROCTALGIA			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	1	1	0

SALIVARY GLAND ENLARGEMENT subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 164 (0.00%) 0	0 / 43 (0.00%) 0
RECTAL HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	4 / 164 (2.44%) 4	1 / 43 (2.33%) 1
STOMATITIS subjects affected / exposed occurrences (all)	9 / 43 (20.93%) 13	28 / 164 (17.07%) 61	8 / 43 (18.60%) 14
VOMITING subjects affected / exposed occurrences (all)	13 / 43 (30.23%) 26	42 / 164 (25.61%) 73	6 / 43 (13.95%) 10
TOOTHACHE subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	7 / 164 (4.27%) 7	1 / 43 (2.33%) 1
Hepatobiliary disorders HYPERBILIRUBINAEMIA subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 2	2 / 164 (1.22%) 3	1 / 43 (2.33%) 1
Skin and subcutaneous tissue disorders BLISTER subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	7 / 164 (4.27%) 7	2 / 43 (4.65%) 2
ALOPECIA subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3	9 / 164 (5.49%) 9	2 / 43 (4.65%) 2
ACNE subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 4	6 / 164 (3.66%) 7	1 / 43 (2.33%) 1
BLOOD BLISTER subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	5 / 164 (3.05%) 5	4 / 43 (9.30%) 4
DERMATITIS subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	3 / 164 (1.83%) 4	1 / 43 (2.33%) 1
DERMATITIS ACNEIFORM			

subjects affected / exposed	2 / 43 (4.65%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	2	4	0
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
DRY SKIN			
subjects affected / exposed	10 / 43 (23.26%)	25 / 164 (15.24%)	7 / 43 (16.28%)
occurrences (all)	13	28	7
ECCHYMOSIS			
subjects affected / exposed	7 / 43 (16.28%)	12 / 164 (7.32%)	0 / 43 (0.00%)
occurrences (all)	10	16	0
ECZEMA			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	4	1
ERYTHEMA			
subjects affected / exposed	2 / 43 (4.65%)	13 / 164 (7.93%)	4 / 43 (9.30%)
occurrences (all)	2	18	6
HYPERHIDROSIS			
subjects affected / exposed	0 / 43 (0.00%)	7 / 164 (4.27%)	3 / 43 (6.98%)
occurrences (all)	0	8	3
NIGHT SWEATS			
subjects affected / exposed	4 / 43 (9.30%)	15 / 164 (9.15%)	3 / 43 (6.98%)
occurrences (all)	5	18	3
NAIL RIDGING			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	3 / 43 (6.98%)
occurrences (all)	1	5	3
HYPERKERATOSIS			
subjects affected / exposed	1 / 43 (2.33%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
ONYCHOCLASIS			
subjects affected / exposed	5 / 43 (11.63%)	22 / 164 (13.41%)	5 / 43 (11.63%)
occurrences (all)	5	23	6
PRURITUS			
subjects affected / exposed	7 / 43 (16.28%)	21 / 164 (12.80%)	2 / 43 (4.65%)
occurrences (all)	9	30	3
PETECHIAE			

subjects affected / exposed	5 / 43 (11.63%)	25 / 164 (15.24%)	3 / 43 (6.98%)
occurrences (all)	6	35	6
PSORIASIS			
subjects affected / exposed	1 / 43 (2.33%)	2 / 164 (1.22%)	1 / 43 (2.33%)
occurrences (all)	2	3	1
RASH			
subjects affected / exposed	5 / 43 (11.63%)	19 / 164 (11.59%)	4 / 43 (9.30%)
occurrences (all)	5	23	5
RASH ERYTHEMATOUS			
subjects affected / exposed	3 / 43 (6.98%)	13 / 164 (7.93%)	4 / 43 (9.30%)
occurrences (all)	5	16	5
RASH MACULAR			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
RASH MACULO-PAPULAR			
subjects affected / exposed	9 / 43 (20.93%)	29 / 164 (17.68%)	10 / 43 (23.26%)
occurrences (all)	12	38	11
SKIN ATROPHY			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	4	1
SKIN FISSURES			
subjects affected / exposed	3 / 43 (6.98%)	9 / 164 (5.49%)	3 / 43 (6.98%)
occurrences (all)	3	9	3
SKIN FRAGILITY			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
SKIN LESION			
subjects affected / exposed	4 / 43 (9.30%)	13 / 164 (7.93%)	3 / 43 (6.98%)
occurrences (all)	7	16	3
SKIN MASS			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	4 / 43 (9.30%)
occurrences (all)	0	5	5
Renal and urinary disorders			

HAEMATURIA			
subjects affected / exposed	3 / 43 (6.98%)	12 / 164 (7.32%)	2 / 43 (4.65%)
occurrences (all)	3	14	2
NEPHROLITHIASIS			
subjects affected / exposed	4 / 43 (9.30%)	6 / 164 (3.66%)	0 / 43 (0.00%)
occurrences (all)	5	7	0
POLLAKIURIA			
subjects affected / exposed	2 / 43 (4.65%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	2	2	0
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	3 / 43 (6.98%)	6 / 164 (3.66%)	1 / 43 (2.33%)
occurrences (all)	3	6	1
Musculoskeletal and connective tissue disorders			
JOINT STIFFNESS			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	2 / 43 (4.65%)
occurrences (all)	1	5	2
FOOT DEFORMITY			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
BONE PAIN			
subjects affected / exposed	5 / 43 (11.63%)	9 / 164 (5.49%)	0 / 43 (0.00%)
occurrences (all)	8	12	0
BACK PAIN			
subjects affected / exposed	11 / 43 (25.58%)	42 / 164 (25.61%)	9 / 43 (20.93%)
occurrences (all)	12	57	14
ARTHRALGIA			
subjects affected / exposed	23 / 43 (53.49%)	82 / 164 (50.00%)	20 / 43 (46.51%)
occurrences (all)	48	162	40
OSTEOARTHRITIS			
subjects affected / exposed	3 / 43 (6.98%)	9 / 164 (5.49%)	2 / 43 (4.65%)
occurrences (all)	3	9	2
NECK PAIN			
subjects affected / exposed	3 / 43 (6.98%)	12 / 164 (7.32%)	3 / 43 (6.98%)
occurrences (all)	3	12	3
MYALGIA			

subjects affected / exposed	9 / 43 (20.93%)	31 / 164 (18.90%)	9 / 43 (20.93%)
occurrences (all)	18	46	11
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 43 (0.00%)	6 / 164 (3.66%)	2 / 43 (4.65%)
occurrences (all)	0	6	2
PAIN IN EXTREMITY			
subjects affected / exposed	5 / 43 (11.63%)	31 / 164 (18.90%)	9 / 43 (20.93%)
occurrences (all)	5	39	12
MUSCLE SPASMS			
subjects affected / exposed	13 / 43 (30.23%)	43 / 164 (26.22%)	11 / 43 (25.58%)
occurrences (all)	20	61	17
PERIARTHRITIS			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
SPINAL PAIN			
subjects affected / exposed	1 / 43 (2.33%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	2	4	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	2 / 43 (4.65%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	2	7	1
CELLULITIS			
subjects affected / exposed	3 / 43 (6.98%)	14 / 164 (8.54%)	7 / 43 (16.28%)
occurrences (all)	3	19	7
CAMPYLOBACTER GASTROENTERITIS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 43 (2.33%)	8 / 164 (4.88%)	2 / 43 (4.65%)
occurrences (all)	2	9	2
EYE INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	7	4
FOLLICULITIS			
subjects affected / exposed	4 / 43 (9.30%)	7 / 164 (4.27%)	2 / 43 (4.65%)
occurrences (all)	10	13	2

FUNGAL SKIN INFECTION			
subjects affected / exposed	3 / 43 (6.98%)	5 / 164 (3.05%)	1 / 43 (2.33%)
occurrences (all)	3	5	1
COVID-19			
subjects affected / exposed	14 / 43 (32.56%)	29 / 164 (17.68%)	13 / 43 (30.23%)
occurrences (all)	18	38	18
CYSTITIS			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	1 / 43 (2.33%)
occurrences (all)	0	3	2
FURUNCLE			
subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
GASTROENTERITIS			
subjects affected / exposed	4 / 43 (9.30%)	8 / 164 (4.88%)	1 / 43 (2.33%)
occurrences (all)	4	8	1
INFLUENZA			
subjects affected / exposed	7 / 43 (16.28%)	13 / 164 (7.93%)	4 / 43 (9.30%)
occurrences (all)	10	16	4
INFECTION			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	0 / 43 (0.00%)	8 / 164 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	9	0
LOCALISED INFECTION			
subjects affected / exposed	4 / 43 (9.30%)	8 / 164 (4.88%)	1 / 43 (2.33%)
occurrences (all)	5	11	1
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	6 / 164 (3.66%)	0 / 43 (0.00%)
occurrences (all)	1	7	0
NASOPHARYNGITIS			
subjects affected / exposed	7 / 43 (16.28%)	26 / 164 (15.85%)	6 / 43 (13.95%)
occurrences (all)	11	33	7
NOROVIRUS INFECTION			

subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 43 (2.33%)	5 / 164 (3.05%)	2 / 43 (4.65%)
occurrences (all)	1	6	3
ORAL HERPES			
subjects affected / exposed	3 / 43 (6.98%)	8 / 164 (4.88%)	2 / 43 (4.65%)
occurrences (all)	5	10	2
OTITIS MEDIA			
subjects affected / exposed	1 / 43 (2.33%)	4 / 164 (2.44%)	3 / 43 (6.98%)
occurrences (all)	1	4	3
PHARYNGITIS			
subjects affected / exposed	0 / 43 (0.00%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
PARONYCHIA			
subjects affected / exposed	5 / 43 (11.63%)	14 / 164 (8.54%)	2 / 43 (4.65%)
occurrences (all)	10	23	2
PNEUMONIA			
subjects affected / exposed	2 / 43 (4.65%)	5 / 164 (3.05%)	2 / 43 (4.65%)
occurrences (all)	2	5	2
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	8 / 164 (4.88%)	6 / 43 (13.95%)
occurrences (all)	5	14	8
PROSTATIC ABSCESS			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	3 / 43 (6.98%)	5 / 164 (3.05%)	0 / 43 (0.00%)
occurrences (all)	5	7	0
SIALOADENITIS			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
TINEA PEDIS			

subjects affected / exposed	0 / 43 (0.00%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	2 / 43 (4.65%)	2 / 164 (1.22%)	0 / 43 (0.00%)
occurrences (all)	2	2	0
SKIN INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	6 / 164 (3.66%)	2 / 43 (4.65%)
occurrences (all)	1	7	3
SINUSITIS			
subjects affected / exposed	7 / 43 (16.28%)	23 / 164 (14.02%)	4 / 43 (9.30%)
occurrences (all)	11	38	7
TOOTH INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	7 / 164 (4.27%)	4 / 43 (9.30%)
occurrences (all)	1	8	5
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	21 / 43 (48.84%)	73 / 164 (44.51%)	22 / 43 (51.16%)
occurrences (all)	44	138	48
URINARY TRACT INFECTION			
subjects affected / exposed	8 / 43 (18.60%)	23 / 164 (14.02%)	6 / 43 (13.95%)
occurrences (all)	15	40	11
VIRAL INFECTION			
subjects affected / exposed	1 / 43 (2.33%)	6 / 164 (3.66%)	1 / 43 (2.33%)
occurrences (all)	1	8	1
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	6 / 43 (13.95%)	19 / 164 (11.59%)	8 / 43 (18.60%)
occurrences (all)	7	23	8
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 43 (0.00%)	0 / 164 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	0 / 43 (0.00%)	4 / 164 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	8	0
HYPERGLYCAEMIA			

subjects affected / exposed	2 / 43 (4.65%)	9 / 164 (5.49%)	6 / 43 (13.95%)
occurrences (all)	3	12	8
HYPERKALAEMIA			
subjects affected / exposed	3 / 43 (6.98%)	12 / 164 (7.32%)	2 / 43 (4.65%)
occurrences (all)	6	15	2
HYPERPHOSPHATAEMIA			
subjects affected / exposed	4 / 43 (9.30%)	8 / 164 (4.88%)	3 / 43 (6.98%)
occurrences (all)	4	11	4
HYPERURICAEMIA			
subjects affected / exposed	7 / 43 (16.28%)	15 / 164 (9.15%)	2 / 43 (4.65%)
occurrences (all)	11	25	2
HYPOCALCAEMIA			
subjects affected / exposed	2 / 43 (4.65%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	2	7	1
HYPOGLYCAEMIA			
subjects affected / exposed	2 / 43 (4.65%)	6 / 164 (3.66%)	0 / 43 (0.00%)
occurrences (all)	2	6	0
HYPOKALAEMIA			
subjects affected / exposed	3 / 43 (6.98%)	11 / 164 (6.71%)	3 / 43 (6.98%)
occurrences (all)	8	20	5
HYPOPHOSPHATAEMIA			
subjects affected / exposed	3 / 43 (6.98%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	3	3	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 43 (0.00%)	1 / 164 (0.61%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
HYPOMAGNESAEMIA			
subjects affected / exposed	3 / 43 (6.98%)	7 / 164 (4.27%)	1 / 43 (2.33%)
occurrences (all)	5	15	1
IRON DEFICIENCY			
subjects affected / exposed	2 / 43 (4.65%)	8 / 164 (4.88%)	3 / 43 (6.98%)
occurrences (all)	2	9	3
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	1 / 43 (2.33%)	3 / 164 (1.83%)	0 / 43 (0.00%)
occurrences (all)	1	3	0

Non-serious adverse events	MRD Cohort: uMRD Not Confirmed (IbrVen->Ibr)	MRD Cohort: uMRD Not Confirmed (IbrVen->IbrVen)	FD Cohort: Reintroduced Ibrutinib
Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 31 (100.00%)	32 / 32 (100.00%)	14 / 18 (77.78%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) SQUAMOUS CELL CARCINOMA subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 18 (5.56%) 1
MELANOCYTIC NAEVUS subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 18 (0.00%) 0
BASAL CELL CARCINOMA subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 5	2 / 32 (6.25%) 2	1 / 18 (5.56%) 1
Vascular disorders HYPERTENSION subjects affected / exposed occurrences (all)	9 / 31 (29.03%) 13	8 / 32 (25.00%) 10	2 / 18 (11.11%) 5
PHLEBITIS subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 32 (6.25%) 2	0 / 18 (0.00%) 0
General disorders and administration site conditions ASTHENIA subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 4	3 / 32 (9.38%) 3	0 / 18 (0.00%) 0
CHEST PAIN subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 32 (3.13%) 1	0 / 18 (0.00%) 0
CHEST DISCOMFORT subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 5	0 / 32 (0.00%) 0	0 / 18 (0.00%) 0
CHILLS subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	4 / 32 (12.50%) 7	0 / 18 (0.00%) 0
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	4 / 31 (12.90%)	1 / 32 (3.13%)	2 / 18 (11.11%)
occurrences (all)	4	1	3
FATIGUE			
subjects affected / exposed	10 / 31 (32.26%)	7 / 32 (21.88%)	1 / 18 (5.56%)
occurrences (all)	22	12	1
MALAISE			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
INJECTION SITE BRUISING			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	4	1	0
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 31 (9.68%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	4	7	0
PERIPHERAL SWELLING			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	2	2	0
PAIN			
subjects affected / exposed	5 / 31 (16.13%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	6	2	0
PYREXIA			
subjects affected / exposed	3 / 31 (9.68%)	10 / 32 (31.25%)	2 / 18 (11.11%)
occurrences (all)	5	13	6
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	2	2	0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
ERECTILE DYSFUNCTION			

subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
TESTICULAR SWELLING			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	8 / 31 (25.81%)	4 / 32 (12.50%)	1 / 18 (5.56%)
occurrences (all)	10	5	1
DYSPNOEA			
subjects affected / exposed	3 / 31 (9.68%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
EPISTAXIS			
subjects affected / exposed	5 / 31 (16.13%)	6 / 32 (18.75%)	2 / 18 (11.11%)
occurrences (all)	8	7	2
HAEMOPTYSIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	9 / 31 (29.03%)	10 / 32 (31.25%)	2 / 18 (11.11%)
occurrences (all)	16	14	3
NASAL DRYNESS			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
NASAL CONGESTION			
subjects affected / exposed	4 / 31 (12.90%)	1 / 32 (3.13%)	2 / 18 (11.11%)
occurrences (all)	4	1	2
SINUS CONGESTION			
subjects affected / exposed	3 / 31 (9.68%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	7 / 31 (22.58%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	7	4	0
DEPRESSION			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
CONFUSIONAL STATE			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
ANXIETY			
subjects affected / exposed	5 / 31 (16.13%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	5	2	1
AGITATION			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	3 / 31 (9.68%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	5	5	0
BLOOD BILIRUBIN INCREASED			

subjects affected / exposed	5 / 31 (16.13%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	17	2	0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 31 (12.90%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	11	5	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 31 (12.90%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	7	5	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	2	4	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			

subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
HAND FRACTURE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
FALL			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
EYE CONTUSION			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
CONTUSION			
subjects affected / exposed	10 / 31 (32.26%)	6 / 32 (18.75%)	1 / 18 (5.56%)
occurrences (all)	14	13	1
LIMB INJURY			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
RIB FRACTURE			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
SCRATCH			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
SKIN ABRASION			
subjects affected / exposed	0 / 31 (0.00%)	6 / 32 (18.75%)	0 / 18 (0.00%)
occurrences (all)	0	7	0
SKIN LACERATION			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
WOUND HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	0	3	2
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	3 / 31 (9.68%)	3 / 32 (9.38%)	2 / 18 (11.11%)
occurrences (all)	3	5	2

PALPITATIONS			
subjects affected / exposed	1 / 31 (3.23%)	6 / 32 (18.75%)	0 / 18 (0.00%)
occurrences (all)	1	8	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
BRAIN FOG			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
HYPOAESTHESIA			
subjects affected / exposed	4 / 31 (12.90%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	6	1	0
HEADACHE			
subjects affected / exposed	8 / 31 (25.81%)	9 / 32 (28.13%)	1 / 18 (5.56%)
occurrences (all)	16	14	2
DYSGEUSIA			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
DIZZINESS			
subjects affected / exposed	5 / 31 (16.13%)	6 / 32 (18.75%)	0 / 18 (0.00%)
occurrences (all)	9	9	0
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
MEMORY IMPAIRMENT			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
PARAESTHESIA			
subjects affected / exposed	4 / 31 (12.90%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	6	2	0
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
SYNCOPE			
subjects affected / exposed	2 / 31 (6.45%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	2	3	1
TREMOR			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	11 / 31 (35.48%)	8 / 32 (25.00%)	1 / 18 (5.56%)
occurrences (all)	19	11	1
ANAEMIA			
subjects affected / exposed	3 / 31 (9.68%)	5 / 32 (15.63%)	2 / 18 (11.11%)
occurrences (all)	7	7	3
LYMPHOCYTOSIS			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
NEUTROPENIA			
subjects affected / exposed	12 / 31 (38.71%)	14 / 32 (43.75%)	0 / 18 (0.00%)
occurrences (all)	29	54	0
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	4	6	0
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 31 (16.13%)	10 / 32 (31.25%)	0 / 18 (0.00%)
occurrences (all)	12	23	0

Ear and labyrinth disorders DEAFNESS NEUROSENSORY subjects affected / exposed occurrences (all) VERTIGO subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0 2 / 31 (6.45%) 2	0 / 32 (0.00%) 0 3 / 32 (9.38%) 4	0 / 18 (0.00%) 0 0 / 18 (0.00%) 0
Eye disorders CONJUNCTIVAL HYPERAEMIA subjects affected / exposed occurrences (all) CATARACT subjects affected / exposed occurrences (all) RETINAL DETACHMENT subjects affected / exposed occurrences (all) DRY EYE subjects affected / exposed occurrences (all) RETINAL TEAR subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) UVEITIS subjects affected / exposed occurrences (all) VITREOUS HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 1 / 31 (3.23%) 1 0 / 31 (0.00%) 0 3 / 31 (9.68%) 3 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0	0 / 32 (0.00%) 0 1 / 32 (3.13%) 1 1 / 32 (3.13%) 1 3 / 32 (9.38%) 3 0 / 32 (0.00%) 0 4 / 32 (12.50%) 4 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0	0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 1 / 18 (5.56%) 2 1 / 18 (5.56%) 1 1 / 18 (5.56%) 3 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 1 / 18 (5.56%) 2
Gastrointestinal disorders ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all) ABDOMINAL DISTENSION	1 / 31 (3.23%) 2	2 / 32 (6.25%) 3	0 / 18 (0.00%) 0

subjects affected / exposed	4 / 31 (12.90%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	4	0	1
ABDOMINAL PAIN			
subjects affected / exposed	2 / 31 (6.45%)	6 / 32 (18.75%)	2 / 18 (11.11%)
occurrences (all)	2	8	2
ABDOMINAL PAIN UPPER			
subjects affected / exposed	7 / 31 (22.58%)	5 / 32 (15.63%)	0 / 18 (0.00%)
occurrences (all)	13	5	0
APHTHOUS ULCER			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
COLITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
CONSTIPATION			
subjects affected / exposed	9 / 31 (29.03%)	6 / 32 (18.75%)	1 / 18 (5.56%)
occurrences (all)	12	10	1
DRY MOUTH			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	23 / 31 (74.19%)	28 / 32 (87.50%)	3 / 18 (16.67%)
occurrences (all)	56	201	6
DYSPEPSIA			
subjects affected / exposed	7 / 31 (22.58%)	7 / 32 (21.88%)	0 / 18 (0.00%)
occurrences (all)	12	7	0
FLATULENCE			
subjects affected / exposed	1 / 31 (3.23%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
DYSPHAGIA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
GASTRITIS			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
HAEMORRHOIDAL HAEMORRHAGE			

subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
GLOSSODYNIA			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
GINGIVAL BLEEDING			
subjects affected / exposed	4 / 31 (12.90%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	5	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	6 / 31 (19.35%)	7 / 32 (21.88%)	2 / 18 (11.11%)
occurrences (all)	9	7	2
HAEMORRHOIDS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
INGUINAL HERNIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
LIP BLISTER			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
MOUTH ULCERATION			
subjects affected / exposed	6 / 31 (19.35%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	10	9	0
ORAL PAIN			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
NAUSEA			
subjects affected / exposed	20 / 31 (64.52%)	12 / 32 (37.50%)	1 / 18 (5.56%)
occurrences (all)	36	22	1
PROCTALGIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

SALIVARY GLAND ENLARGEMENT			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 31 (0.00%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
STOMATITIS			
subjects affected / exposed	6 / 31 (19.35%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	11	20	0
VOMITING			
subjects affected / exposed	7 / 31 (22.58%)	11 / 32 (34.38%)	0 / 18 (0.00%)
occurrences (all)	16	14	0
TOOTHACHE			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
BLISTER			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
ALOPECIA			
subjects affected / exposed	0 / 31 (0.00%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
ACNE			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
BLOOD BLISTER			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
DERMATITIS ACNEIFORM			

subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
DRY SKIN			
subjects affected / exposed	3 / 31 (9.68%)	5 / 32 (15.63%)	1 / 18 (5.56%)
occurrences (all)	3	5	1
ECCHYMOSIS			
subjects affected / exposed	3 / 31 (9.68%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	4	2	0
ECZEMA			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
ERYTHEMA			
subjects affected / exposed	2 / 31 (6.45%)	5 / 32 (15.63%)	0 / 18 (0.00%)
occurrences (all)	4	6	0
HYPERHIDROSIS			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
NIGHT SWEATS			
subjects affected / exposed	5 / 31 (16.13%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	6	4	1
NAIL RIDGING			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
HYPERKERATOSIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
ONYCHOCLASIS			
subjects affected / exposed	5 / 31 (16.13%)	6 / 32 (18.75%)	0 / 18 (0.00%)
occurrences (all)	5	6	0
PRURITUS			
subjects affected / exposed	3 / 31 (9.68%)	8 / 32 (25.00%)	0 / 18 (0.00%)
occurrences (all)	4	13	0
PETECHIAE			

subjects affected / exposed	6 / 31 (19.35%)	8 / 32 (25.00%)	0 / 18 (0.00%)
occurrences (all)	9	11	0
PSORIASIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
RASH			
subjects affected / exposed	3 / 31 (9.68%)	6 / 32 (18.75%)	0 / 18 (0.00%)
occurrences (all)	5	7	0
RASH ERYTHEMATOUS			
subjects affected / exposed	2 / 31 (6.45%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	2	3	0
RASH MACULAR			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
RASH MACULO-PAPULAR			
subjects affected / exposed	5 / 31 (16.13%)	5 / 32 (15.63%)	0 / 18 (0.00%)
occurrences (all)	9	6	0
SKIN ATROPHY			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
SKIN DISCOLOURATION			
subjects affected / exposed	3 / 31 (9.68%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
SKIN FISSURES			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
SKIN FRAGILITY			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
SKIN LESION			
subjects affected / exposed	1 / 31 (3.23%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	1	4	0
SKIN MASS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

HAEMATURIA			
subjects affected / exposed	3 / 31 (9.68%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	5	4	0
NEPHROLITHIASIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
POLLAKIURIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
JOINT STIFFNESS			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
FOOT DEFORMITY			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
BONE PAIN			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
BACK PAIN			
subjects affected / exposed	10 / 31 (32.26%)	9 / 32 (28.13%)	2 / 18 (11.11%)
occurrences (all)	17	11	5
ARTHRALGIA			
subjects affected / exposed	17 / 31 (54.84%)	16 / 32 (50.00%)	2 / 18 (11.11%)
occurrences (all)	28	34	3
OSTEOARTHRITIS			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
NECK PAIN			
subjects affected / exposed	3 / 31 (9.68%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	3	2	0
MYALGIA			

subjects affected / exposed	7 / 31 (22.58%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	8	3	1
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 31 (0.00%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
PAIN IN EXTREMITY			
subjects affected / exposed	8 / 31 (25.81%)	8 / 32 (25.00%)	3 / 18 (16.67%)
occurrences (all)	8	13	3
MUSCLE SPASMS			
subjects affected / exposed	10 / 31 (32.26%)	7 / 32 (21.88%)	1 / 18 (5.56%)
occurrences (all)	11	11	1
PERIARTHRITIS			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
SPINAL PAIN			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
CELLULITIS			
subjects affected / exposed	0 / 31 (0.00%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	0	9	0
CAMPYLOBACTER GASTROENTERITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	2	2	1
EYE INFECTION			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
FOLLICULITIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

FUNGAL SKIN INFECTION			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	3 / 18 (16.67%)
occurrences (all)	2	0	4
CYSTITIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
FURUNCLE			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
GASTROENTERITIS			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
INFLUENZA			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	2 / 31 (6.45%)	5 / 32 (15.63%)	1 / 18 (5.56%)
occurrences (all)	2	5	1
LOCALISED INFECTION			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	4	1	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 31 (12.90%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
NASOPHARYNGITIS			
subjects affected / exposed	8 / 31 (25.81%)	5 / 32 (15.63%)	0 / 18 (0.00%)
occurrences (all)	9	6	0
NOROVIRUS INFECTION			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
ORAL HERPES			
subjects affected / exposed	0 / 31 (0.00%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	0	3	1
OTITIS MEDIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
PARONYCHIA			
subjects affected / exposed	3 / 31 (9.68%)	4 / 32 (12.50%)	1 / 18 (5.56%)
occurrences (all)	3	8	2
PNEUMONIA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
PROSTATIC ABSCESS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
RHINITIS			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
SIALOADENITIS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
TINEA PEDIS			

subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
SKIN INFECTION			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
SINUSITIS			
subjects affected / exposed	7 / 31 (22.58%)	4 / 32 (12.50%)	1 / 18 (5.56%)
occurrences (all)	11	8	1
TOOTH INFECTION			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	14 / 31 (45.16%)	11 / 32 (34.38%)	2 / 18 (11.11%)
occurrences (all)	24	15	2
URINARY TRACT INFECTION			
subjects affected / exposed	6 / 31 (19.35%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	8	6	1
VIRAL INFECTION			
subjects affected / exposed	1 / 31 (3.23%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	2	4	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	4 / 31 (12.90%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	6	2	0
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
GOUT			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	4	3	0
HYPERGLYCAEMIA			

subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
HYPERKALAEMIA			
subjects affected / exposed	4 / 31 (12.90%)	3 / 32 (9.38%)	0 / 18 (0.00%)
occurrences (all)	4	3	0
HYPERPHOSPHATAEMIA			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
HYPERURICAEMIA			
subjects affected / exposed	1 / 31 (3.23%)	4 / 32 (12.50%)	1 / 18 (5.56%)
occurrences (all)	2	7	1
HYPOCALCAEMIA			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
HYPOGLYCAEMIA			
subjects affected / exposed	3 / 31 (9.68%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
HYPOKALAEMIA			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	3	3	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
HYPONATRAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	2	7	1
IRON DEFICIENCY			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	1	3	1
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	FD Cohort: Reintroduced Ibr+Ven	MRD Cohort: Reintroduced Ibrutinib	MRD Cohort: Reintroduced Ven + Continued Ibr
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	5 / 7 (71.43%)	2 / 2 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	5 / 11 (45.45%)	3 / 7 (42.86%)	0 / 2 (0.00%)
occurrences (all)	7	4	0
PHLEBITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
FATIGUE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
MALAISE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE BRUISING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
TESTICULAR SWELLING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	0 / 11 (0.00%)	2 / 7 (28.57%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
DYSPNOEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
HAEMOPTYSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
PRODUCTIVE COUGH			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
NASAL DRYNESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
AGITATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
BLOOD BILIRUBIN INCREASED			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HAND FRACTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
EYE CONTUSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RIB FRACTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SCRATCH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN ABRASION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
SKIN LACERATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
WOUND HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

PALPITATIONS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
BRAIN FOG			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
TREMOR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
ANAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
LYMPHOCYTOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0

Ear and labyrinth disorders DEAFNESS NEUROSENSORY subjects affected / exposed occurrences (all) VERTIGO subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1 0 / 11 (0.00%) 0	0 / 7 (0.00%) 0 0 / 7 (0.00%) 0	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0
Eye disorders CONJUNCTIVAL HYPERAEMIA subjects affected / exposed occurrences (all) CATARACT subjects affected / exposed occurrences (all) RETINAL DETACHMENT subjects affected / exposed occurrences (all) DRY EYE subjects affected / exposed occurrences (all) RETINAL TEAR subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) UVEITIS subjects affected / exposed occurrences (all) VITREOUS HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0
Gastrointestinal disorders ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all) ABDOMINAL DISTENSION	0 / 11 (0.00%) 0 	0 / 7 (0.00%) 0 	0 / 2 (0.00%) 0

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
APHTHOUS ULCER			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
COLITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
DRY MOUTH			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	4 / 11 (36.36%)	2 / 7 (28.57%)	2 / 2 (100.00%)
occurrences (all)	7	3	3
DYSPEPSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDAL HAEMORRHAGE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GLOSSODYNIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	2
HAEMORRHOIDS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
INGUINAL HERNIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
LIP BLISTER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
MOUTH ULCERATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	3	0	1
PROCTALGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

SALIVARY GLAND ENLARGEMENT			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
TOOTHACHE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
BLISTER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ALOPECIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
BLOOD BLISTER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
DERMATITIS ACNEIFORM			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
DRY SKIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
ECCHYMOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
NAIL RIDGING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPERKERATOSIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
ONYCHOCLASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
PETECHIAE			

subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
PSORIASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RASH MACULAR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN ATROPHY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN FISSURES			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN FRAGILITY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN LESION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
SKIN MASS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

HAEMATURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
POLLAKIURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
JOINT STIFFNESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
FOOT DEFORMITY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
BONE PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
BACK PAIN			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
ARTHRALGIA			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
MYALGIA			

subjects affected / exposed	2 / 11 (18.18%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	2 / 11 (18.18%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
PERIARTHROSITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SPINAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CELLULITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
CAMPYLOBACTER GASTROENTERITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
CONJUNCTIVITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
EYE INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
FOLLICULITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	2 / 11 (18.18%)	3 / 7 (42.86%)	1 / 2 (50.00%)
occurrences (all)	2	4	1
CYSTITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
FURUNCLE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
HERPES ZOSTER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
LOCALISED INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
NOROVIRUS INFECTION			

subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
ORAL HERPES			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PARONYCHIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
PNEUMONIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
PROSTATIC ABSCESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SIALOADENITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
TINEA PEDIS			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
SKIN INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
SINUSITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
TOOTH INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 11 (18.18%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	2	2	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
VIRAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
HYPERGLYCAEMIA			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPERKALAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPERPHOSPHATAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPERURICAEMIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2017	<p>Protocol Amendment 1</p> <p>Summary of Changes:</p> <ul style="list-style-type: none">• Defined MRD cohort and added a FD cohort study to evaluate the depth of response after 15 months fixed duration of therapy, in addition to the current MRD cohort assessing discontinuation based on MRD status.• Included contraception up to 90 days for women of child-bearing age post-treatment in order to align with both venetoclax and ibrutinib products' current labelling.• Excluded subjects with uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenia purpura.• Included updates to align language with current version of the ibrutinib IB.
29 November 2018	<p>Protocol Amendment 2</p> <p>Summary of Changes:</p> <ul style="list-style-type: none">• Included collection and storage of imaging for the MRD cohort in addition to the FD cohort.• Included collection of BM slides for the FD cohort in addition to the MRD cohort.• Combined endpoints for the MRD cohort pre-randomization and randomization phases.• Added DOR and TLS risk reduction as secondary endpoints.• Updated concomitant use with CYP3A inhibitor section.• Included updates to align language with the current ibrutinib IB.
11 September 2019	<p>Protocol Amendment 3</p> <p>Summary of Changes:</p> <ul style="list-style-type: none">• Extended duration of study to enable extended follow-up in the FD cohort.• Increased frequency of efficacy assessment visits without CT scans in FD cohort.• Clarified duration of therapy and duration of study for the MRD cohort.• Clarified timing of primary analyses for FD and MRD cohorts.• Clarified choice and duration of reintroduction therapy for both MRD and FD cohorts.• Reduced frequency of both reintroduction visits and CT scans, CT assessments in response to follow-up visits.• Clarified response to ibrutinib reintroduction as an exploratory endpoint in the MRD and FD cohorts.• Added an additional MRD assessment (added Cycle 28 in FD cohort) and additional biomarker assessments.
02 December 2022	<p>Protocol Amendment 4</p> <p>Summary of Changes:</p> <ul style="list-style-type: none">• Extended study duration to enable longer follow-up in the FD cohort.• Included other editorial and administrative changes.• Include the updated recommendations that are intended to improve tolerability for continued ibrutinib treatment in the study protocol.• Update risks to cardiac arrhythmia section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported