



Clinical trial results: A Phase-Ib/II Study of Ruxolitinib and Pomalidomide Combination Therapy in Patients with Primary and Secondary Myelofibrosis Summary

EudraCT number	2012-002431-29
Trial protocol	DE
Global end of trial date	27 April 2024

Results information

Result version number	v1 (current)
This version publication date	10 May 2025
First version publication date	10 May 2025
Summary attachment (see zip file)	MPNSG_02-12_Final_report_BfArM_22Apr2025_final_version (MPNSG_02-12_Final_report_BfArM_22Apr2025_final_version.pdf)

Trial information

Trial identification

Sponsor protocol code	POMINC(MPNSG02-12)
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01644110
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital of Ulm
Sponsor organisation address	Albert-Einstein-Allee 23, Ulm, Germany, 89081
Public contact	Clinical trials office IM III, University Hospital of Ulm, +49 73150045901, mpnsg.innere3@uniklinik-ulm.de
Scientific contact	Clinical trials office IM III, University Hospital of Ulm, +49 73150045901, mpnsg.innere3@uniklinik-ulm.de

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	03 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2024
Global end of trial reached?	Yes
Global end of trial date	27 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the clinical efficacy of ruxolitinib and pomalidomide combination therapy in primary and secondary MF patients based on the consensus criteria of the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) (Tefferi A et al, 2006), extended by the criterion RBC-transfusion independence (RBC-TI) (Gale RP et al, 2011; Gale RP et al, 2012).

Protection of trial subjects:

Safety was assessed by evaluation the following: reported adverse events, clinical laboratory test results, vital signs measurements, ECG findings, chest X-ray, sonographic assessment of the spleen, physical examination findings, monitoring of concomitant medications. For each safety parameter, all findings whether normal or abnormal were recorded in the CRF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 95
Worldwide total number of subjects	95
EEA total number of subjects	95

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)	17
From 65 to 84 years	77

85 years and over	1
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Subject disposition

Recruitment

Recruitment details:

First patient in: 19 Aug 2013; Last patient in: 27 April 2021; last patient out: 27 April 2024; Interruption after 6 patients in April 2014 for safety analysis. Restart of recruitment in July 2014. 2nd interruption in February 2017 until approval of amended protocol version 2.0. Restart of recruitment in August 2017.

Pre-assignment

Screening details:

Diagnosis of myeloproliferative neoplasms (de novo or secondary (post PV or post ET)), anemia with hemoglobin < 10g/dl or transfusion-dependent anemia, splenomegaly > 11cm total diameter and/or leukoerythroblastosis, ECOG < 3

Pre-assignment period milestones

Number of subjects started	95
Number of subjects completed	92

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 3
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Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

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

Dosage and administration details:

1 capsule of 0,5 mg per day for 12 cycles

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

Dosage and administration details:

2 capsules of 5 mg twice daily at treatment start, escalation of 5 mg twice daily allowed after 4 weeks if platelet counts stable or increasing, maximum dosage 25 mg twice daily. For 12 cycles

Arm title	Cohort 2
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Arm description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

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

Dosage and administration details:

1 capsule of 0,5 mg (cycles 1-3), 1 mg (cycles 4-6) or 2 mg (start in cycle 7) per day for 12 cycles

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

Dosage and administration details:

2 capsules of 5 mg twice daily at treatment start, escalation of 5 mg twice daily allowed after 4 weeks if platelet counts stable or increasing, maximum dosage 25 mg twice daily. For 12 cycles

Number of subjects in period 1^[1]	Cohort 1	Cohort 2
Started	39	53
Completed	27	31
Not completed	12	22
Adverse event, serious fatal	3	3
Consent withdrawn by subject	3	6
Adverse event, non-fatal	1	6
Progress of underlying disease	3	1
Transplantation	1	-
Lack of efficacy	1	6

Notes:

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

Justification: 95 patients started with screening but only 92 were included into the treatment arms. 3 patients were screening failure due to protocol deviation.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

Reporting group title	Cohort 2
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Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	39	53	92
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	10	17
From 65-84 years	32	42	74
85 years and over	0	1	1
Age continuous			
Units: years			
median	72	70	
full range (min-max)	49 to 83	52 to 86	-
Gender categorical			
Units: Subjects			
Female	17	21	38
Male	22	32	54
Type of myelofibrosis			
Units: Subjects			
Primary MF	30	34	64
Secondary MF	9	18	27
Unclassified MF	0	1	1
Bone marrow fibrosis grade			
Units: Subjects			
Grade 0	0	1	1
Grade 1	5	4	9
Grade 2	14	25	39

Grade 3	15	20	35
Missing	5	3	8
ECOG			
Units: Subjects			
ECOG 0	12	25	37
ECOG 1	25	25	50
ECOG 2	1	3	4
Missing	1	0	1
Pretreated			
Pretreatment with any medications for myelofibrosis			
Units: Subjects			
yes	22	33	55
no	17	20	37
Pretreated with Ruxolitinib			
Units: Subjects			
yes	6	23	29
no	33	30	63
RBC transfusion dependent			
Units: Subjects			
yes	10	19	29
no	29	34	63
JAK2V617F Mutation			
Is a JAK2V617F Mutation available?			
Units: Subjects			
yes	28	25	53
no	11	28	39
MPL Mutation			
Is a MPM Mutation available?			
Units: Subjects			
yes	3	8	11
no	36	45	81
CALR Mutation			
Is a CALR Mutation available?			
Units: Subjects			
yes	8	14	22
no	30	39	69
Missing	1	0	1
Baseline DIPSS			
Units: Subjects			
Low	1	0	1
Intermediate - 1	6	5	11
Intermediate - 2	27	39	66
High	5	9	14
Any high risk mutation			
Is there any high risk mutation available (ASXL1, EZH2, SRSF2, IDH1+2, U2AF1, TP53)?			
Units: Subjects			
yes	25	31	56
no	14	22	36
ASXL1 Mutation			
Units: Subjects			
Yes	16	22	38

No	23	31	54
EZH2 Mutation			
Units: Subjects			
Yes	4	7	11
No	35	46	81
SRSF2 Mutation			
Units: Subjects			
Yes	9	13	22
No	30	40	70
IDH2 Mutation			
Units: Subjects			
Yes	1	7	8
No	38	46	84
U2AF1 Mutation			
Units: Subjects			
Yes	5	7	12
No	34	46	80
TP53 Mutation			
Units: Subjects			
Yes	3	1	4
No	36	52	88
Baseline spleen ultrasound			
Units: cm			
median	17.9	17.0	
full range (min-max)	12.6 to 28.0	11.4 to 36.0	-
Baseline spleen palpation			
Units: cm			
median	5.0	3.0	
full range (min-max)	0 to 22.0	0 to 22.0	-
Baseline hemoglobin value			
Units: g/dl			
median	8.6	8.6	
full range (min-max)	5.4 to 11.7	5.9 to 10.8	-
MPN SAF Baseline			
Mean values of selected questions of the Quality of Life Questionnaire MPN-SAF.			
Units: Points			
arithmetic mean	2.98	2.62	
standard deviation	± 1.68	± 1.82	-
Baseline thrombocytes value			
Units: Giga/l			
median	249	247	
full range (min-max)	88 to 787	86 to 1240	-
MIPSS			
Mutation-enhanced international prognostic score system			
Units: points			
median	3	3	
full range (min-max)	1 to 3	1 to 3	-

End points

End points reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

Reporting group title	Cohort 2
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Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

Subject analysis set title	Intention-to-treat
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Includes all patients who received the study medication at least once.

Primary: Response after 12 cycles

End point title	Response after 12 cycles
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End point description:

Response was defined according to the IWG-MRT criteria (including complete remission, partial remission, clinical improvement), stable disease (Tefferi A et al, 2006), and red cell transfusion according to Gale et al 2010 and 2011, also progressive disease, relapse disease

End point type	Primary
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End point timeframe:

The end point disease response was examined at the end of each cycle until at least cycle 12.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	53		
Units: Subjects				
Complete remission	0	0		
Partial remission	1	0		
Clinical improvement	6	4		
Progressive disease	1	0		
Relapse disease	2	0		
Red blood cell transfusion dependent	4	6		
Red blood cell transfusion independent	1	2		
Clinical benefit	0	16		
Missing	13	23		
Stable disease	11	2		

Statistical analyses

Statistical analysis title	Rate of response
Statistical analysis description: For cohort 1, response was defined as complete remission, partial remission, clinical improvement and red blood cell transfusion independency. For cohort 2, response was defined as complete remission, partial remission, clinical improvement and red blood cell transfusion independency, stable disease and clinical improvement.	
Comparison groups	Cohort 2 v Cohort 1
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other ^[1]
Method	Binomialtest
Parameter estimate	Estimated response rate
Point estimate	0.453
Confidence interval	
level	95 %
sides	1-sided
lower limit	0.335

Notes:

[1] - For cohort 1, Simon's 2 stage design was used for analysis. The estimated response rate was 0.205 with one-sided 90% CI [0.123, 1].

According to amendment 2, additional 53 subjects was included as cohort 2 to decide whether the proportion responding, P, is less than or equal to 0.300 (null hypothesis) or greater than or equal to 0.500 (alternative). For cohort 2, a binomial test was used.

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Secondary
End point timeframe:	
Overall Survival: Number of patients and events by cohort with median survival time in months.	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	53		
Units: months				
median (confidence interval 95%)	38.4 (29.8 to 100)	60.8 (29.8 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival
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End point description:

End point type	Secondary
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End point timeframe:

Progression free survival: Number of patients and events by cohort with median survival time in months

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	53		
Units: months				
median (confidence interval 95%)	29.8 (16.4 to 43)	34.3 (21.2 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration or response

End point title	Duration or response
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End point description:

End point type	Secondary
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End point timeframe:

Duration of response from first response to loss of response (if occurred) or until end-of-FU (if no loss occurred)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	53		
Units: cycles				
median (full range (min-max))	15 (8 to 126)	9 (2 to 77)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from Informed Consent signature up to 28 days after last study drug administration or until all drug-related toxicities had been resolved, whichever was later.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	3.0
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Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

All patients treated cohort 1

Reporting group title	Cohort 2
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Reporting group description:

All patients treated in cohort 2

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 39 (76.92%)	35 / 53 (66.04%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events	6	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	6 / 39 (15.38%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 6	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Fibrosarcoma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Second primary malignancy alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Surgical and medical procedures			
Breast operation			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint arthroplasty			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden cardiac death			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chest pain			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	3 / 39 (7.69%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pain alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Reproductive system and breast disorders Acquired hydrocele alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders Dyspnoea alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemorrhage			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Myocardial infarction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac valve disease			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiorenal syndrome			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endocarditis fibroplastica			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Cerebral ischaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral sensory neuropathy			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haemorrhage			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenomegaly			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spontaneous haematoma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders Deafness alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 39 (2.56%) 0 / 1 0 / 0	0 / 53 (0.00%) 0 / 0 0 / 0	
Gastrointestinal disorders Abdominal pain alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 39 (5.13%) 0 / 2 0 / 0	0 / 53 (0.00%) 0 / 0 0 / 0	
Ascites alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 39 (2.56%) 0 / 1 0 / 1	0 / 53 (0.00%) 0 / 0 0 / 0	
Diarrhoea alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0	1 / 53 (1.89%) 0 / 1 0 / 0	
Gastrointestinal haemorrhage alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0	2 / 53 (3.77%) 0 / 2 0 / 1	
Large intestine perforation alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0	1 / 53 (1.89%) 0 / 1 0 / 0	
Nausea alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatotoxicity			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Soft tissue necrosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cystitis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nasopharyngitis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 39 (2.56%) 0 / 1 0 / 0	 0 / 53 (0.00%) 0 / 0 0 / 0		
Oral viral infection alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 39 (0.00%) 0 / 0 0 / 0	 1 / 53 (1.89%) 1 / 1 0 / 0		
Peritonitis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 39 (0.00%) 0 / 0 0 / 0	 1 / 53 (1.89%) 0 / 1 0 / 0		
Pneumonia alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 5 / 39 (12.82%) 0 / 5 0 / 2	 6 / 53 (11.32%) 4 / 7 1 / 1		
Sepsis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 2 / 39 (5.13%) 0 / 2 0 / 2	 1 / 53 (1.89%) 1 / 1 0 / 0		
Septic shock alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 39 (2.56%) 0 / 1 0 / 1	 0 / 53 (0.00%) 0 / 0 0 / 0		
Skin infection alternative dictionary used: MedDRA 27.0				

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 39 (97.44%)	53 / 53 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Dermatology - Other (Basal cell carcinoma)			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	3	1	
Dermatology - Other (Spinaliom)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Secondary Malignancy (possibly related to cancer treatment)	Additional description: basal cell carcinoma		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Sexual - Other (cyst right ovary)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Vascular disorders			
Hematoma			
subjects affected / exposed	3 / 39 (7.69%)	5 / 53 (9.43%)	
occurrences (all)	7	6	
Hemorrhage - Other (defecation - black dyed)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Hemorrhage - Other (eye)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Hemorrhage - Other (Gums)			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Hemorrhage - Other (tongue)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Hemorrhage -Other (spitting of blood)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Hemorrhage pulmonary - Nose		
subjects affected / exposed	4 / 39 (10.26%)	2 / 53 (3.77%)
occurrences (all)	9	2
Hemorrhage with surgery		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Hemorrhage, GI - Oral cavity		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Hemorrhage, GU		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Thrombosis/embolism (vascular access)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Thrombosis/thrombus/embolism		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Vascular - Other (atherosklerotic artery on both sides)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Vascular - Other (circumference increase leg left)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Vasculitis		

subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Vein injury - Extremity (lower)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Constitutional Symptoms - Other (exhaustion)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (General disorder)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (physical ability decreased)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (reduced constitutional behavior)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (reduced exercise capacity)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (Reduced general condition)			
subjects affected / exposed	4 / 39 (10.26%)	0 / 53 (0.00%)	
occurrences (all)	4	0	
Constitutional Symptoms - Other (Vitamin D3 deficiency)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Constitutional Symptoms - Other (Weakness)			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Fatigue			

subjects affected / exposed occurrences (all)	16 / 39 (41.03%) 24	12 / 53 (22.64%) 13	
Fever subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 5	8 / 53 (15.09%) 14	
Insomnia subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4	2 / 53 (3.77%) 2	
Rigors/chills subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 3	1 / 53 (1.89%) 1	
Sweating subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 4	3 / 53 (5.66%) 3	
Weight gain subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 53 (3.77%) 2	
Immune system disorders Allergic reaction subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Allergy - Other (vaccination reaction) subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Rhinitis subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	3 / 53 (5.66%) 3	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 39 (17.95%) 8	8 / 53 (15.09%) 12	
Dyspnea subjects affected / exposed occurrences (all)	12 / 39 (30.77%) 19	21 / 53 (39.62%) 31	
Hypoxia			

subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Nasal/paranasal reactions			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	2	
Pain - Chest/thorax NOS			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Pain - Other (Chest wall)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pain Pulmonary/Upper Respiratory: Chest/thorax NOS			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Pain Pulmonary/Upper Respiratory: Throat/pharynx/larynx			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	3 / 39 (7.69%)	1 / 53 (1.89%)	
occurrences (all)	3	1	
Pulmonary - Other (breath sound)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pulmonary - Other (bronchitis)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pulmonary - Other (influenza)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pulmonary - Other (Pneumonia NOS)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Cardiac General - Other (Cardiac decompensation)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Valvular heart disease		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Edema: trunk/genital		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Intraop injury - Artery-aorta		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Left ventricular systolic dysfunction		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Supraventricular arrhythmia - Atrial fibrillation		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Cardiac General - Other (cardiac insufficiency)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Cardiac General - Other (coronary artery disease)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Cardiac General - Other (Edema pulmonary)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Cardiac General - Other (Edema)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Cardiac General - Other (heart insufficiency)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0

Conduction abnormality - AV block second degree			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pain Cardiavascular: Cardiac/heart			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Palpitations			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Supraventricular arrhythmia - Sinus bradycardia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Cardiac Arrhythmia - Other (Arrhythmia)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Cardiac General - Other (cardiopulmonal congestion)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Cardiac General - Other (increased heart rate)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Cardiac General - Other (drop in blood pressure)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Conduction abnormality - AV Block-Third degree (Complete AV Block)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Edema: Head and neck			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Hypotension			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Edema: limb			
subjects affected / exposed	1 / 39 (2.56%)	4 / 53 (7.55%)	
occurrences (all)	1	5	
Hypertension			
subjects affected / exposed	4 / 39 (10.26%)	3 / 53 (5.66%)	
occurrences (all)	4	3	
Pulmonary hypertension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ventricular arrhythmia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Apnea			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Confusion			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	11 / 39 (28.21%)	10 / 53 (18.87%)	
occurrences (all)	16	11	
Mood alteration - Depression			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Mood alteration			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Neurology - Other (Concentration problem)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	2	
Neurology - Other (Dysesthesia)			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Neurology - Other (Panic attack)		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Neurology - Other (Paresthesia)		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Neurology - Other (Polyneuropathy)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Neurology - Other (speaking disorder)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Neurology - Other (Spinal disc herniation)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Neurology - Other (Tingling in feet)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Neuropathy - sensory		
subjects affected / exposed	3 / 39 (7.69%)	10 / 53 (18.87%)
occurrences (all)	3	10
Pain Neurology: Head/headache		
subjects affected / exposed	6 / 39 (15.38%)	5 / 53 (9.43%)
occurrences (all)	8	7
Pain Neurology: Neuralgia/peripheral nerve		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Syncope (fainting)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Tremor		

subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	4	
Blood and lymphatic system disorders			
Hemoglobin			
subjects affected / exposed	17 / 39 (43.59%)	23 / 53 (43.40%)	
occurrences (all)	21	29	
Platelets			
subjects affected / exposed	6 / 39 (15.38%)	8 / 53 (15.09%)	
occurrences (all)	9	10	
Blood - Other (leukocytosis)			
subjects affected / exposed	2 / 39 (5.13%)	2 / 53 (3.77%)	
occurrences (all)	4	2	
Blood - Other (Splenomegaly)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Hemolysis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Coagulation - Other (von Willebrandt syndrome type 2)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Iron overload			
subjects affected / exposed	1 / 39 (2.56%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
Neutrophils			
subjects affected / exposed	1 / 39 (2.56%)	8 / 53 (15.09%)	
occurrences (all)	1	8	
Blood - Other (Thrombocytosis)			
subjects affected / exposed	3 / 39 (7.69%)	3 / 53 (5.66%)	
occurrences (all)	4	3	
Blood - Other (eosinophilia)			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Blood - Other (Blasts)			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	2	
Blood - Other (Hematocrit decreased)			
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
Coagulation - Other (Coagulation disorder)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
INR			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Leukocytes			
subjects affected / exposed	0 / 39 (0.00%)	4 / 53 (7.55%)	
occurrences (all)	0	4	
Lymphatics - Other (Lymphnodes)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Blood - Other (red blood cells decreased)			
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Auditory/Ear - Other (Ear noises			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Hearing (without monitoring program)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pain Auditory/Ear: External ear			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Eye disorders			

Blurred vision			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	2	
Dry eye			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Glaucoma			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ocular - Other (Eye irritation)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ocular - Other (Herpes eye)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ocular - Other (Swollen eyes)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ocular - Other (Swollen tear sac)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ocular surface disease			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Watery eye			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Anorexia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Ascites			
subjects affected / exposed	3 / 39 (7.69%)	1 / 53 (1.89%)	
occurrences (all)	3	1	
Colitis			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Constipation		
subjects affected / exposed	6 / 39 (15.38%)	12 / 53 (22.64%)
occurrences (all)	8	12
Diarrhea		
subjects affected / exposed	9 / 39 (23.08%)	15 / 53 (28.30%)
occurrences (all)	11	21
Distension		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Dry mouth		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Dysphagia		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Flatulence		
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	3
Gastritis		
subjects affected / exposed	1 / 39 (2.56%)	5 / 53 (9.43%)
occurrences (all)	1	5
Gastrointestinal - Other (loss of appetite)		
subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)
occurrences (all)	2	1
Gastrointestinal - Other (abdominal problems)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	2	0
Gastrointestinal - Other (Condylomas)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	2
Gastrointestinal - Other (Gastroenteritis)		

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Gastrointestinal - Other (unspecific symptoms)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Heartburn		
subjects affected / exposed	2 / 39 (5.13%)	7 / 53 (13.21%)
occurrences (all)	2	7
Mucositis (clinical exam) - Pharynx		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Mucositis (clinical exam) - Oral cavity		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Nausea		
subjects affected / exposed	5 / 39 (12.82%)	5 / 53 (9.43%)
occurrences (all)	5	6
Pain Gastrointestinal: Abdomen NOS		
subjects affected / exposed	7 / 39 (17.95%)	3 / 53 (5.66%)
occurrences (all)	13	9
Pain Gastrointestinal: Dental/teeth/periodontal		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Pain Gastrointestinal: Oral cavity		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Pain Gastrointestinal: stomach		
subjects affected / exposed	1 / 39 (2.56%)	4 / 53 (7.55%)
occurrences (all)	3	4
Taste alteration		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Teeth		

subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	3 / 53 (5.66%) 4	
Teeth development subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4	7 / 53 (13.21%) 9	
Hepatobiliary disorders Hepatobiliary - Other (Steatosis) subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Pain Hepatobiliary/Pancreas: Liver subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 53 (3.77%) 2	
Bruising subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 2	0 / 53 (0.00%) 0	
Decubitus subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Dermatology - Other (perioral efflorescence) subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Dermatology - Other (diaper rash) subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Dermatology - Other (eczema) subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Dermatology - Other (Erysipel face)			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Dermatology - Other (excision of skin change)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Dermatology - Other (furuncle right buttock)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Dermatology - Other (Herpes zoster)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Dermatology - Other (Skin changes)		
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	3
Dermatology - Other (skin lesion)		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Dermatology - Other (swelling of lower leg)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Dry skin		
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	3
Flushing		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Injection site reaction		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Pruritus		
subjects affected / exposed	3 / 39 (7.69%)	2 / 53 (3.77%)
occurrences (all)	4	2
Rash		

subjects affected / exposed	2 / 39 (5.13%)	2 / 53 (3.77%)	
occurrences (all)	2	3	
Ulceration			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	3 / 39 (7.69%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Pain - Renal/Genitourinary - Kidney			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Renal - Other (Chronic kidney disease)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Renal - Other (chronic renal insufficiency)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Renal - Other (fluid retention)			
subjects affected / exposed	7 / 39 (17.95%)	9 / 53 (16.98%)	
occurrences (all)	9	10	
Renal - Other (fluid retention/ edema)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Renal - Other (Prostata adenoma)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Renal - Other (recurrent dysuria)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Renal - Other (Renal stricture)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
renal - other (urinary obstruction)			

subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 53 (0.00%) 0	
Renal failure subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	1 / 53 (1.89%) 1	
Urinary frequency subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 2	3 / 53 (5.66%) 4	
Urinary retention subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	1 / 53 (1.89%) 1	
Endocrine disorders Endocrine - Other (partially hemorrhagic cyst) subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Endocrine - Other (Struma multinodosa) subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Hot flashes subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Hypothyroidism subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	3 / 53 (5.66%) 3	
Musculoskeletal and connective tissue disorders Fracture subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 53 (3.77%) 2	
Joint - function subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Muscle weakness subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 53 (1.89%) 1	
Musculoskeletal - Other (arthrosis			

left knee)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal - Other (bone pain, hip pain)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Musculoskeletal - Other (Bursitis)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Musculoskeletal - Other (Cervicobrachialgie)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal - Other (coxarthrosis)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal - Other (Cramps calves)			
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal - Other (Cramps)			
subjects affected / exposed	15 / 39 (38.46%)	14 / 53 (26.42%)	
occurrences (all)	20	16	
Musculoskeletal - Other (disc herniation)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal - Other (hernia)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Musculoskeletal - Other (Lockjaw)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Musculoskeletal - Other (muscle tension neck)			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	

Musculoskeletal - Other (muscle tensions)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Musculoskeletal - Other (spasms)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Musculoskeletal - Other (Swelling ankle)		
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	2
Musculoskeletal - Other (Tendon rupture)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Musculoskeletal - Other (tension right shoulder)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Pain - Other (Flank right)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Pain - Other (Groin)		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Pain - Other (jaw)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Pain - Other (left axilla)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Pain - Other (leg)		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Pain Musculoskeletal: Back		
subjects affected / exposed	5 / 39 (12.82%)	8 / 53 (15.09%)
occurrences (all)	7	8
Pain Musculoskeletal: Bone		

subjects affected / exposed	5 / 39 (12.82%)	4 / 53 (7.55%)	
occurrences (all)	11	4	
Pain Musculoskeletal: Buttock			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Pain Musculoskeletal: Extremity- limb			
subjects affected / exposed	5 / 39 (12.82%)	1 / 53 (1.89%)	
occurrences (all)	9	1	
Pain Musculoskeletal: Joint			
subjects affected / exposed	8 / 39 (20.51%)	14 / 53 (26.42%)	
occurrences (all)	8	16	
Pain Musculoskeletal: Muscle			
subjects affected / exposed	5 / 39 (12.82%)	3 / 53 (5.66%)	
occurrences (all)	10	3	
Pain Musculoskeletal: Neck			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Flu-like syndrome			
subjects affected / exposed	4 / 39 (10.26%)	1 / 53 (1.89%)	
occurrences (all)	6	1	
Infection - Other (Abscess)			
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
Infection - Other (aspiration pneumonia)			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Infection - Other (common cold)			
subjects affected / exposed	8 / 39 (20.51%)	6 / 53 (11.32%)	
occurrences (all)	11	10	
Infection - Other (COVID 19 Infection)			
subjects affected / exposed	2 / 39 (5.13%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Infection - Other (erysipiel)			

subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (Follikulitis)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (foot)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection - Other (General, Blood)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection - Other (Herpes zoster)		
subjects affected / exposed	4 / 39 (10.26%)	2 / 53 (3.77%)
occurrences (all)	5	3
Infection - Other (Left digitus medius)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (phlegmon)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (Pneumonia)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (Sepsis)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection - Other (Skin)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection - Other (sore throat)		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Infection - Other (Urosepsis)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1

Infection - Other (wound)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection with grade 3 or 4 neutrophils- Liver		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with grade 3 or 4 neutrophils- pharynx		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection with grade 3 or 4 neutrophils		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with grade 3 or 4 neutrophils- Urinary tract NOS		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with normal ANC		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with normal ANC - Upper airway NOS		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with unknown ANC - Bronchus		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Infection with unknown ANC - pharynx		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection with unknown ANC - Upper airway NOS		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection with unknown ANC - Urinary tract NOS		

subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Infection Dermatology/Skin: Lip/perioral		
subjects affected / exposed	2 / 39 (5.13%)	2 / 53 (3.77%)
occurrences (all)	2	2
Infection Gastrointestinal: Abdomen NOS		
subjects affected / exposed	5 / 39 (12.82%)	6 / 53 (11.32%)
occurrences (all)	6	6
Infection Gastrointestinal: Dental- tooth		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Infection Gastrointestinal: Oral cavity-gums (gingivitis)		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection Musculoskeletal: Joint		
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)
occurrences (all)	1	1
Infection Ocular: Conjunctiva		
subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)
occurrences (all)	2	1
Infection Ocular: Eye NOS		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Infection Pulmonary/Upper Respiratory: Bronchus		
subjects affected / exposed	7 / 39 (17.95%)	3 / 53 (5.66%)
occurrences (all)	8	3
Infection Pulmonary/Upper Respiratory: Lung (pneumonia)		
subjects affected / exposed	0 / 39 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	3
Infection Pulmonary/Upper Respiratory: Pharynx		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1

Infection Pulmonary/Upper Respiratory: Sinus			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Infection Pulmonary/Upper Respiratory: Upper aerodigestive NOS			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Infection Pulmonary/Upper Respiratory: Upper airway NOS			
subjects affected / exposed	3 / 39 (7.69%)	13 / 53 (24.53%)	
occurrences (all)	6	14	
Infection Renal/Genitourinary: Bladder (urinary)			
subjects affected / exposed	1 / 39 (2.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Infection Renal/Genitourinary: Prostate			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Infection Renal/Genitourinary: Urinary tract NOS			
subjects affected / exposed	5 / 39 (12.82%)	8 / 53 (15.09%)	
occurrences (all)	6	9	
Infection Sexual/Reproductive Function: Pelvis NOS			
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
ALT			
subjects affected / exposed	4 / 39 (10.26%)	1 / 53 (1.89%)	
occurrences (all)	5	1	
AST			
subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
Cholesterol			
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Creatinine			

subjects affected / exposed	9 / 39 (23.08%)	2 / 53 (3.77%)
occurrences (all)	9	3
GGT		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Hyperkalemia		
subjects affected / exposed	2 / 39 (5.13%)	1 / 53 (1.89%)
occurrences (all)	2	1
Hyperuricemia		
subjects affected / exposed	8 / 39 (20.51%)	6 / 53 (11.32%)
occurrences (all)	9	6
Hypoalbuminemia		
subjects affected / exposed	0 / 39 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	1
Hypocalcemia		
subjects affected / exposed	2 / 39 (5.13%)	0 / 53 (0.00%)
occurrences (all)	2	0
Hypokalemia		
subjects affected / exposed	2 / 39 (5.13%)	2 / 53 (3.77%)
occurrences (all)	2	2
Metabolic/Lab - Other (Hyperphosphatemia)		
subjects affected / exposed	1 / 39 (2.56%)	0 / 53 (0.00%)
occurrences (all)	1	0
Metabolic/Lab - Other (Iron deficiency)		
subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	2
Metabolic/Lab - Other (LDH increase)		
subjects affected / exposed	1 / 39 (2.56%)	3 / 53 (5.66%)
occurrences (all)	1	3
Metabolic/Lab - Other (Urea high)		
subjects affected / exposed	3 / 39 (7.69%)	0 / 53 (0.00%)
occurrences (all)	4	0
Metabolic/Lab - Other (Vitamin D deficiency)		

subjects affected / exposed	0 / 39 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2013	Urgent Amendment: Ruxolitinib was initially dispensed in bottles. This urgent amendment was necessary as Ruxolitinib was not available in bottles anymore but only in blisters. The urgent amendment was implemented in protocol version 1.4
16 April 2014	Amendment 1.4 (07.01.2024): Exclusion Criteria added "Patient treatment with Ruxolitinib within a 14 days time period before Screening phase"; Implementation of tuberculosis tests; bone marrow biopsy and aspiration obtained at baseline, end of cycle 6, end of cycle 12 (biopsy: reference lab Hannover and Freiburg, aspiration: reference lab Ulm); Ruxolitinib dispensed in blisters (see also urgent amendment); parameter haptoglobin added.
06 June 2017	Amendment V 2.0 (28.03.2017): cohort 2 implemented: Pomalidomid 0,5 mg for 3 cycles, afterwards 1 mg for 3 cycles, starting cycle 7 2 mg; no change for Ruxolitinib; sample size increased: cohort 2 intended patient sample size n=53; study end changed to May 2022; explorative response criteria clinical benefit added; pregnancy prevention plan updated; Pomalidomid will be dispensed in wallets, not in bottles anymore.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 March 2014	The POMINC study was interrupted for a safety analysis after enrollment of 6 patients and an observation period of each patient of at least one cycles (28 days) on 25-Mar-2014. This was outlined in the protocol (12.3.4). As the LKP, the trial coordinator, the statistician and the DSMB didn't have any safety concerns the study restarted recruitment on 02-Jul-2014	02 July 2014

Notes:

Limitations and caveats

None reported