Clinical trial results:
A phase II Study of the Efficacy and Safety of lenalidomide, subcutaneous bortezomib, and dexamethasone combination therapy for patients with newly diagnosed multiple myeloma

Summary

EudraCT number	2013-005008-32
Trial protocol	IE
Global end of trial date	31 October 2024

Results information

Result version number	v1 (current)
This version publication date	24 December 2025
First version publication date	24 December 2025

Trial information

Trial identification

Sponsor protocol code	CTRIAL (ICORG) 13-17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02219178
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	RCSI House, 121 St. Stephen's Green, Dublin, Ireland, D02 H903
Public contact	Clinical Trials Information, Cancer Trials Ireland, +353 16677211, info@cancertrials.ie
Scientific contact	Clinical Trials Information, Cancer Trials Ireland, +353 16677211, info@cancertrials.ie

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	23 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2019
Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the overall response rate after 4 cycles and the best response to induction therapy with combination of lenalidomide, subcutaneous bortezomib, and dexamethasone (RsqVD) in patients with newly diagnosed multiple myeloma.

Protection of trial subjects:

The study was conducted in accordance with the EU Directive 2001/20/EC and International Conference on Harmonisation (ICH) for Good Clinical Practice (GCP) and the ethical principles founded in the Declaration of Helsinki.
All regulatory requirements were followed, and appropriate study documentation was reviewed by the competent authority/ ethics committee in order to safeguard the rights, safety and well-being of the patients.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	28 November 2014
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	Ireland: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	21
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is an open label, single arm phase II study that planned to enroll up to 42 eligible patients with newly diagnosed multiple myeloma in Ireland.
42 patients were registered on the study from 28-Nov-2024 to 29-Feb-2016.

Pre-assignment

Screening details:

Patients with newly diagnosed multiple myeloma, who met all of the inclusion criteria and none of the exclusion criteria were eligible for enrollment in this study.

Period 1

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

Arms

Arm title	Single Arm

Arm description:

Combination of Lenalidomide + Subcutaneous Bortezomib + Dexamethasone

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

Dosage and administration details:

Lenalidomide will be given as a single daily oral dose (25mg) on days 1-14 followed by a 7-day rest period.

On commencement of maintenance therapy, patients who have undergone transplantation will receive lenalidomide at 10 mg administered days 1-21 of each 28 day cycle starting at approximately 3 months post-transplant. If the 10 mg dose is tolerated well, the dose of lenalidomide will be increased to 15 mg after three 28 day cycles of maintenance.

Patients who do not undergo transplantation will receive lenalidomide at the same dose taken in the final cycle of induction provided this dose was tolerated well, administered days 1 – 21 of each 28 day cycle.

Lenalidomide capsules should be swallowed whole, and should not be broken, chewed or opened. Administration of lenalidomide will be at approximately the same time each day. Drug may be taken with or without food.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	Velcade
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Bortezomib (1.3 mg/m2) will be administered subcutaneously on days 1, 4, 8, and 11 followed by a 10-day rest period during induction cycles. Each induction cycle has a duration of 21 days.

Patients with high-risk disease will receive bortezomib during the maintenance period, with subcutaneous bortezomib 1.3 mg/m2 days 1 and 15 of each 28-day maintenance cycle.

All patients on maintenance treatment will complete an end of treatment/study withdrawal visit by 31 October 2019 and continue with treatment as per standard of care.
Drug to be administered under supervision of the investigator/sub-investigator.

The amount (in mg) of drug to be administered will be determined based on Body Surface Area (BSA).

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

Dosage and administration details:

Dexamethasone will be given as a single daily oral dose on days 1, 2, 4, 5, 8, 9, 11 and 12, followed by a 9-day rest period during induction cycles only. All participants will receive a dexamethasone dose of 20 mg.

Dexamethasone should be taken at approximately the same time each day. It is recommended that dexamethasone be taken in the morning to reduce insomnia. Each dose should be taken with food. Drug diary provided to participants to record oral administration of doses.

Number of subjects in period 1	Single Arm
Started	42
Completed	31
Not completed	11
Physician decision	1
Participant decided to withdraw from the study	4
Failed criterion for study eligibility	1
Death	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study (overall period)

Reporting group description: -

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	42	42	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	21	21	
From 65-84 years	21	21	
85 years and over	0	0	
Age continuous Units: years			
median	64		
full range (min-max)	45 to 79	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	27	27	
Durie Salmon Stage at Initial Diagnosis			
Recorded for Full Analysis Set (N=37 patients who were eligible for the study and had at least 2 cycles of study treatment)			
Units: Subjects			
Missing	5	5	
IA	3	3	
IIA	11	11	
IIB	1	1	
IIIA	16	16	
IIIB	1	1	
Not Recorded	5	5	
ISS Grade at Initial Diagnosis			
Recorded for Full Analysis Set (N=37 patients who were eligible for the study and had at least 2 cycles of study treatment)			
Units: Subjects			
Grade I	15	15	
Grade II	13	13	
Grade III	9	9	
Not recorded	5	5	

Time from Initial Diagnosis to First Study Treatment Units: Weeks median full range (min-max)		- -	

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Consists of 37 patients who were eligible for the study and had at least two cycles of study treatment. One ineligible patient (creatinine clearance at screening was < 45 ml/min) and four patients who only had one cycle of study treatment were excluded.
All efficacy analyses are performed for the FAS

Reporting group values	Full Analysis Set		
Number of subjects	37		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female Male			
Durie Salmon Stage at Initial Diagnosis			
Recorded for Full Analysis Set (N=37 patients who were eligible for the study and had at least 2 cycles of study treatment)			
Units: Subjects			
Missing IA IIA IIB IIIA IIIB Not Recorded	5 3 11 1 16 1		
ISS Grade at Initial Diagnosis			
Recorded for Full Analysis Set (N=37 patients who were eligible for the study and had at least 2 cycles of study treatment)			
Units: Subjects			

Grade I	15		
Grade II	13		
Grade III	9		
Not recorded			
Time from Initial Diagnosis to First Study Treatment			
Units: Weeks			
median	2.1		
full range (min-max)	0.3 to 15.7		

End points

End points reporting groups

Reporting group title	Single Arm

Reporting group description:

Combination of Lenalidomide + Subcutaneous Bortezomib + Dexamethasone

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Consists of 37 patients who were eligible for the study and had at least two cycles of study treatment. One ineligible patient (creatinine clearance at screening was < 45 ml/min) and four patients who only had one cycle of study treatment were excluded.
All efficacy analyses are performed for the FAS

Primary: Overall response rate (ORR) after 4 induction cycles

End point title	Overall response rate (ORR) after 4 induction cycles[1]

End point description:

The ORR after 4 induction cycles was 91.9%, with a CI of [78.1 – 98.3], and a CR/VGPR rate of 59.5%. The lower bound of the CI exceeds the ORR of 70% as pre-specified in the assumptions for the sample size calculation.

End point type	Primary

End point timeframe:

Overall response rate (ORR) after 4 induction cycles, defined as Complete Response (CR) or Stringent Complete Response (SCR) or Very Good Partial Response (VGPR) or Partial Response (PR).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: % of Participants				
number (not applicable)				
Complete Response (CR)	8.1			
Very Good Partial Response (VGPR)	51.4			
Partial Response (PR)	32.4			
Stable Disease	2.7			
Progressive Disease	5.4			

Statistical analyses

No statistical analyses for this end point

Primary: Overall response rate (ORR) at End of Induction

End point title	Overall response rate (ORR) at End of Induction[2]

End point description:

The ORR at the end of induction therapy was also 91.9%, with a CI of [78.1 – 98.3], and a CR/VGPR rate of 62.2%.

End point type	Primary

End point timeframe:

Overall response rate (ORR) at end of induction, defined as Complete Response (CR) or Stringent Complete Response (SCR) or Very Good Partial Response (VGPR) or Partial Response (PR)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: % of patients				
number (not applicable)				
Complete Response (CR)	8.1			
Very Good Partial Response (VGPR)	54.1			
Partial Response (PR)	29.7			
Stable Disease	2.7			
Progressive Disease	5.4			

Statistical analyses

No statistical analyses for this end point

Primary: Best Response Rate During Induction

End point title	Best Response Rate During Induction[3]

End point description:

The best ORR during induction therapy was 94.6%, with a CI of [81.8 – 99.3], and a CR/VGPR rate of 62.2%.

End point type	Primary

End point timeframe:

Best response to induction therapy, defined as Complete Response (CR) or Stringent Complete Response (SCR) or Very Good Partial Response (VGPR) or Partial Response (PR).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: % of patients				
number (not applicable)				
Complete Response (CR)	8.1			
Very Good Partial Response (VGPR)	54.1			
Partial Response (PR)	32.4			
Stable Disease	5.4			

Statistical analyses

No statistical analyses for this end point

Primary: Best Response During Study Treatment

End point title	Best Response During Study Treatment[4]

End point description:

The best ORR during the entire study treatment period was also 94.6%, with a CI of [81.8 – 99.3], an SCR/CR/VGPR rate of 75.6% and an SCR/CR rate of 43.2%

End point type	Primary

End point timeframe:

Best Response During Study Treatment defined as Complete Response (CR) or Stringent Complete Response (SCR) or Very Good Partial Response (VGPR) or Partial Response (PR)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: % of patients				
number (not applicable)				
Stringent Complete Response (SCR)	18.9			
Complete Response (CR)	24.3			
Very Good Partial Response (VGPR)	32.4			
Partial Response (PR)	18.9			
Stable Disease	5.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression during Study Treatment

End point title	Progression during Study Treatment

End point description:

Only six patients progressed on study treatment, so the median time to progression was not estimable. Only the lower bound for the 95% confidence interval for median TTP can be estimated (as 2.8 years). Patients who have not progressed or died are censored at the date last known to be progression-free. Should a patient be progression-free at end of study treatment, TTP will be censored at the most recent prior response assessment.
Median Time to Progression (years) Inestimable
95% CI for Median Time to Progression [2.8 - Inestimable]

End point type	Secondary

End point timeframe:

Time to progression (TTP), defined as the length of time between the date of registration and date of disease progression, with death before progression censored at date of death.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: % of patients				
number (not applicable)				
Progressed on Study Treatment	16.2			
Censored	83.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Status After One Year on Study Treatment

End point title	Progression-Free Status After One Year on Study Treatment

End point description:

Six patients discontinued study treatment before one year for reasons other than progression, leaving 31 patients assessable for progression-free status. Three patients progressed before completing a year on study treatment and 28 patients (90.3%, 95% CI of [74.2% - 98.0%]) were progression-free after one year on study treatment.
Patients who have not progressed or died are censored at the date last known to be progression-free. Should a patient be progression-free at end of study treatment, PFS will be censored at the most recent prior response assessment.

End point type	Secondary

End point timeframe:

Progression-free survival (PFS), defined as the length of time between the date of registration and the earliest date of disease progression or death due to any cause.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	37[5]			
Units: % of patients				
number (not applicable)				
Progressed Before One Year	9.7			
Progression-Free at One Year	90.3			

Notes:

[5] - Six patients discontinued study treatment before one year for reasons other than progression.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment Emergent Adverse Events	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Group 1
Reporting group description: -	

Serious adverse events	Group 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 42 (69.05%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer metastatic	Additional description: Colon cancer metastatic		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Metastatic malignant melanoma	Additional description: Metastatic malignant melanoma		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse	Additional description: Circulatory collapse		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension	Additional description: Hypertension		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hernia repair	Additional description: Hernia repair		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stoma closure	Additional description: Stoma closure		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal operation	Additional description: Spinal operation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain	Additional description: Pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Multiple organ dysfunction syndrome	Additional description: Multiple organ dysfunction syndrome		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis	Additional description: Atelectasis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cough	Additional description: Cough		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lung consolidation	Additional description: Lung consolidation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Delirium	Additional description: Delirium		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state	Additional description: Confusional state		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Fibrin D dimer increased	Additional description: Fibrin D dimer increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Facial bones fracture	Additional description: Facial bones fracture		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall	Additional description: Fall		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest	Additional description: Cardio-respiratory arrest		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness	Additional description: Dizziness		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Headache	Additional description: Headache		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope	Additional description: Presyncope		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Syncope	Additional description: Syncope		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation	Additional description: Disseminated intravascular coagulation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia	Additional description: Neutropenia		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal vein occlusion	Additional description: Retinal vein occlusion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Enteritis	Additional description: Enteritis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		

Gastritis	Additional description: Gastritis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation	Additional description: Constipation		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation	Additional description: Large intestine perforation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Melaena	Additional description: Melaena		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea	Additional description: Nausea		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Hypersensitivity vasculitis	Additional description: Hypersensitivity vasculitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash	Additional description: Rash		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure	Additional description: Renal failure		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment	Additional description: Renal impairment		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain	Additional description: Back pain		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		

Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Campylobacter gastroenteritis	Additional description: Campylobacter gastroenteritis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary sepsis	Additional description: Biliary sepsis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear infection	Additional description: Ear infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious	Additional description: Diarrhoea infectious		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
H1N1 influenza	Additional description: H1N1 influenza		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis B	Additional description: Hepatitis B		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious colitis	Additional description: Infectious colitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease	Additional description: Infective exacerbation of chronic obstructive airways disease		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza	Additional description: Influenza		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Laryngitis	Additional description: Laryngitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Listeriosis	Additional description: Listeriosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		

subjects affected / exposed	6 / 42 (14.29%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral	Additional description: Lower respiratory tract infection viral		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences causally related to treatment / all	6 / 7		
deaths causally related to treatment / all	0 / 0		
Otitis media acute	Additional description: Otitis media acute		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis	Additional description: Neutropenic sepsis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media	Additional description: Otitis media		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection	Additional description: Respiratory tract infection		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia	Additional description: Hyponatraemia		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophagia	Additional description: Hypophagia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Group 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Dysplastic naevus	Additional description: Dysplastic naevus		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Flushing	Additional description: Flushing		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hot flush	Additional description: Hot flush		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypertension	Additional description: Hypertension		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Hypotension	Additional description: Hypotension		

subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	7		
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Phlebitis	Additional description: Phlebitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Raynaud's phenomenon	Additional description: Raynaud's phenomenon		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Varicose vein	Additional description: Varicose vein		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Surgical and medical procedures			
Cataract operation	Additional description: Cataract operation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin graft	Additional description: Skin graft		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tooth extraction	Additional description: Tooth extraction		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Tooth repair	Additional description: Tooth repair		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Chest pain	Additional description: Chest pain		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Chills	Additional description: Chills		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cyst	Additional description: Cyst		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	25 / 42 (59.52%)		
occurrences (all)	45		
Gait disturbance	Additional description: Gait disturbance		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hernia pain	Additional description: Hernia pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	8		
Injection site bruising	Additional description: Injection site bruising		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Injection site pain	Additional description: Injection site pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Injection site rash	Additional description: Injection site rash		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Malaise	Additional description: Malaise		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Mucosal inflammation	Additional description: Mucosal inflammation		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	3		
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	19		
Pain	Additional description: Pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	15		
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	17		
Immune system disorders			
Allergy to arthropod sting	Additional description: Allergy to arthropod sting		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Breast tenderness	Additional description: Breast tenderness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Perineal erythema	Additional description: Perineal erythema		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
subjects affected / exposed	19 / 42 (45.24%)		
occurrences (all)	50		
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	13		
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hiccups	Additional description: Hiccups		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Obstructive airways disorder	Additional description: Obstructive airways disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	23		
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Productive cough	Additional description: Productive cough		

subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	8		
Pulmonary congestion	Additional description: Pulmonary congestion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Rales	Additional description: Rales		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Rhinitis allergic	Additional description: Rhinitis allergic		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tachypnoea	Additional description: Tachypnoea		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Wheezing	Additional description: Wheezing		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Psychiatric disorders			
Abnormal dreams	Additional description: Abnormal dreams		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Anxiety	Additional description: Anxiety		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	8		
Confusional state	Additional description: Confusional state		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Delirium	Additional description: Delirium		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		

Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Depression	Additional description: Depression		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Depressive symptom	Additional description: Depressive symptom		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Insomnia	Additional description: Insomnia		
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	13		
Libido decreased	Additional description: Libido decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Mood altered	Additional description: Mood altered		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Nightmare	Additional description: Nightmare		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Restlessness	Additional description: Restlessness		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Sleep disorder	Additional description: Sleep disorder		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Investigations			
Adjusted calcium decreased	Additional description: Adjusted calcium decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	14		
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		

subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	7		
Biopsy skin	Additional description: Biopsy skin		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood albumin decreased	Additional description: Blood albumin decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	3		
Blood cholesterol increased	Additional description: Blood cholesterol increased		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	9		
Blood folate decreased	Additional description: Blood folate decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood glucose decreased	Additional description: Blood glucose decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood magnesium decreased	Additional description: Blood magnesium decreased		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	6		
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	5		
Blood pressure increased	Additional description: Blood pressure increased		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Body mass index increased	Additional description: Body mass index increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Breath sounds abnormal	Additional description: Breath sounds abnormal		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Ejection fraction decreased	Additional description: Ejection fraction decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	9		
Heart rate irregular	Additional description: Heart rate irregular		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
International normalised ratio increased	Additional description: International normalised ratio increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	3		
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Liver function test increased	Additional description: Liver function test increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Neutrophil count decreased	Additional description: Neutrophil count decreased		

subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	36		
Neutrophil count increased	Additional description: Neutrophil count increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	9		
Wound healing normal	Additional description: Wound healing normal		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	23		
Weight increased	Additional description: Weight increased		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	11		
White blood cell count increased	Additional description: White blood cell count increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Troponin increased	Additional description: Troponin increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Excoriation	Additional description: Excoriation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Fall	Additional description: Fall		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Foot fracture	Additional description: Foot fracture		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Laceration	Additional description: Laceration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Limb injury	Additional description: Limb injury		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Muscle strain	Additional description: Muscle strain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nasal injury	Additional description: Nasal injury		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Post operative Ileus	Additional description: Post operative Ileus		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin abrasion	Additional description: Skin abrasion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin laceration	Additional description: Skin laceration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Soft tissue injury	Additional description: Soft tissue injury		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Sunburn	Additional description: Sunburn		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tooth fracture	Additional description: Tooth fracture		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Upper limb fracture	Additional description: Upper limb fracture		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Wound	Additional description: Wound		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nervous system disorders			
Amnesia	Additional description: Amnesia		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Burning feet syndrome	Additional description: Burning feet syndrome		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dizziness	Additional description: Dizziness		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Cerebral infarction	Additional description: Cerebral infarction		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dysaesthesia	Additional description: Dysaesthesia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Headache	Additional description: Headache		

subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	10		
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lethargy	Additional description: Lethargy		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hyporeflexia	Additional description: Hyporeflexia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Memory impairment	Additional description: Memory impairment		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Migraine	Additional description: Migraine		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	15 / 42 (35.71%)		
occurrences (all)	27		
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	7		
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	17		
Presyncope	Additional description: Presyncope		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Retinal migraine	Additional description: Retinal migraine		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Sciatica	Additional description: Sciatica		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Somnolence	Additional description: Somnolence		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Taste disorder	Additional description: Taste disorder		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Tremor	Additional description: Tremor		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	28		
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	65		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	15		
Ear and labyrinth disorders			
Deafness	Additional description: Deafness		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Ear congestion	Additional description: Ear congestion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Ear pain	Additional description: Ear pain		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypoacusis	Additional description: Hypoacusis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Vertigo	Additional description: Vertigo		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Eye disorders			
Asthenopia	Additional description: Asthenopia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blepharitis	Additional description: Blepharitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cataract	Additional description: Cataract		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dry eye	Additional description: Dry eye		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Conjunctival haemorrhage	Additional description: Conjunctival haemorrhage		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Erythema of eyelid	Additional description: Erythema of eyelid		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye discharge	Additional description: Eye discharge		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye disorder	Additional description: Eye disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		

Eye pain	Additional description: Eye pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Eyelid ptosis	Additional description: Eyelid ptosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Myopia	Additional description: Myopia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Macular degeneration	Additional description: Macular degeneration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Ocular hyperaemia	Additional description: Ocular hyperaemia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	9		
Photophobia	Additional description: Photophobia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Vision blurred	Additional description: Vision blurred		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	5		
Abdominal pain upper	Additional description: Abdominal pain upper		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Anal incontinence	Additional description: Anal incontinence		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Constipation	Additional description: Constipation		
subjects affected / exposed	20 / 42 (47.62%)		
occurrences (all)	31		
Dental caries	Additional description: Dental caries		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	28 / 42 (66.67%)		
occurrences (all)	74		
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Flatulence	Additional description: Flatulence		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Gastric dilatation	Additional description: Gastric dilatation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Gastritis	Additional description: Gastritis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Gastrointestinal wall thickening	Additional description: Gastrointestinal wall thickening		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lip swelling	Additional description: Lip swelling		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Mouth ulceration	Additional description: Mouth ulceration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nausea	Additional description: Nausea		
subjects affected / exposed	19 / 42 (45.24%)		
occurrences (all)	31		
Oral disorder	Additional description: Oral disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Oral pain	Additional description: Oral pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Toothache	Additional description: Toothache		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Tongue discolouration	Additional description: Tongue discolouration		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	18		
Hepatobiliary disorders			
Cholecystitis	Additional description: Cholecystitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cholelithiasis	Additional description: Cholelithiasis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne	Additional description: Acne		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	3		
Dermal cyst	Additional description: Dermal cyst		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Drug eruption	Additional description: Drug eruption		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Ecchymosis	Additional description: Ecchymosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Erythema	Additional description: Erythema		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Dry skin	Additional description: Dry skin		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Hyperhidrosis	Additional description: Hyperhidrosis		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Lipohypertrophy	Additional description: Lipohypertrophy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Miliaria	Additional description: Miliaria		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nail ridging	Additional description: Nail ridging		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Night sweats	Additional description: Night sweats		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Petechiae	Additional description: Petechiae		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pigmentation disorder	Additional description: Pigmentation disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pruritus	Additional description: Pruritus		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Pruritus generalised	Additional description: Pruritus generalised		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Purpura	Additional description: Purpura		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rash	Additional description: Rash		
subjects affected / exposed	17 / 42 (40.48%)		
occurrences (all)	22		
Rash generalised	Additional description: Rash generalised		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rash macular	Additional description: Rash macular		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	15		
Rash papular	Additional description: Rash papular		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Skin disorder	Additional description: Skin disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Skin reaction	Additional description: Skin reaction		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Stasis dermatitis	Additional description: Stasis dermatitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Urticaria	Additional description: Urticaria		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Renal and urinary disorders			
Chromaturia	Additional description: Chromaturia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Chronic kidney disease	Additional description: Chronic kidney disease		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cystitis haemorrhagic	Additional description: Cystitis haemorrhagic		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nocturia	Additional description: Nocturia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		

Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	17		
Back pain	Additional description: Back pain		
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	26		
Bone pain	Additional description: Bone pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Bone swelling	Additional description: Bone swelling		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Bursitis	Additional description: Bursitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Flank pain	Additional description: Flank pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Groin pain	Additional description: Groin pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Joint Effusion	Additional description: Joint Effusion		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Joint range of motion decreased	Additional description: Joint range of motion decreased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	8		
Limb discomfort	Additional description: Limb discomfort		

subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Muscle fatigue	Additional description: Muscle fatigue		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	14		
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Musculoskeletal discomfort	Additional description: Musculoskeletal discomfort		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	8		
Musculoskeletal stiffness	Additional description: Musculoskeletal stiffness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Myalgia	Additional description: Myalgia		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Osteoarthritis	Additional description: Osteoarthritis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Osteonecrosis of jaw	Additional description: Osteonecrosis of jaw		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	20		
Pain in jaw	Additional description: Pain in jaw		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rotator cuff syndrome	Additional description: Rotator cuff syndrome		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Infections and infestations			
Aspergillus infection	Additional description: Aspergillus infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	6		
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Conjunctivitis viral	Additional description: Conjunctivitis viral		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Ear infection	Additional description: Ear infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Enterococcal infection	Additional description: Enterococcal infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye infection	Additional description: Eye infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Fungal infection	Additional description: Fungal infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		

Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hordeolum	Additional description: Hordeolum		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Influenza	Additional description: Influenza		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Laryngitis	Additional description: Laryngitis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Infected dermal cyst	Additional description: Infected dermal cyst		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Infection	Additional description: Infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Listeriosis	Additional description: Listeriosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	38		
Lower respiratory tract infection viral	Additional description: Lower respiratory tract infection viral		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	17 / 42 (40.48%)		
occurrences (all)	38		
Onychomycosis	Additional description: Onychomycosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		

Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Pharyngitis	Additional description: Pharyngitis		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Pharyngitis streptococcal	Additional description: Pharyngitis streptococcal		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	11		
Respiratory tract infection viral	Additional description: Respiratory tract infection viral		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	15		
Skin candida	Additional description: Skin candida		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tonsillitis	Additional description: Tonsillitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tooth abscess	Additional description: Tooth abscess		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tooth infection	Additional description: Tooth infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		

Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	32		
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Viral infection	Additional description: Viral infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Viral upper respiratory tract infection	Additional description: Viral upper respiratory tract infection		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Vulvitis	Additional description: Vulvitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Acidosis	Additional description: Acidosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	16		
Dehydration	Additional description: Dehydration		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Fluid overload	Additional description: Fluid overload		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	6		
Hypercholesterolaemia	Additional description: Hypercholesterolaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hyperkalaemia	Additional description: Hyperkalaemia		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Hypernatraemia	Additional description: Hypernatraemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	4		
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	19		
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Hypophagia	Additional description: Hypophagia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	14		
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2014	Protocol Version 2_25Aug2014 Updates included: - Revision of Exclusion Criteria #20 - Revision of Haematological Toxicities Platelet Count - Revision of Adverse Events List for Lenalidomide - Revision of Lenolidamide Risks and SAE reporting - Administrative changes to protocol - Updates to resolve minor protocol inconsistencies.
29 October 2014	Protocol Version 3_17Oct2014 Updates included: - Clarification on the Lenalidomide dosing regimen for patients who undergo transplantation - Updated Study Schema for clarity - Updated Study Calendar
22 April 2015	Protocol Version 4_07April2015 Updates included: - Added reference to Bortezomib SPC - Updated inclusion criteria number 2 - Updated Study Calendar - Updated Study Schema - Added RsqVD Substudy details - Added additional method of submitting SAE reports - Other administration changes
28 October 2015	Protocol Version 5_23Sep2015 Updates included - Change to protocol that stem cell collection is not mandatory. - Updated Inclusion Criteria Number 1 - Update to Inclusion Criteria Number 5 - Added Inclusion Criteria Number 9 - Updates to Section 12 Study Calendar - Deletion of Appendix I - Clarification of sentence in relation to Bortezomib dosing - Updates to Section 12 Study Calendar - Updates to Section 17 Safety - Updates to Appendix J
25 April 2016	Protocol Version 6_02Feb2016 Updates inlcuded: - Administrative change to criteria of removal from study due to consent withdrawal. - Clarification on concomitant medications to be recorded during the study - Revised definition of evaluable for response. - Clarification of data to be included in efficacy analysis and safety analysis. - Clarification of SAE reporting procedure to pharmaceutical manufacturers of Investigational Medicinal Products.
07 September 2016	Protocol Version 7_08Jun2016 Updates included: - Change of sub study contact details - Update that central review is now planned for response assessments - Correction to creatinine clearance formulas

30 July 2019	Protocol Version _13Jun2019 Updates included: -Administrative changes -Update to maintenance cycles -Secondary objectives updated to clarify that safety of induction therapy and maintenance therapy is evaluated. -Clarification on sub-study sample collection -Survival data post EOT -Confirmation of follow up duration -Confirmation of EOS enrolment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported