Clinical trial results:
A Phase 3, Randomized, Controlled, Open-label Study of VELCADE (Bortezomib) Melphalan-Prednisone (VMP) Compared to Daratumumab in Combination with VMP (D-VMP), in Subjects with Previously Untreated Multiple Myeloma who are Ineligible for High-dose Therapy

Summary

EudraCT number	2014-002272-88
Trial protocol	HU BE ES CZ IT DE BG RO PL HR GR PT
Global end of trial date	07 August 2024

Results information

Result version number	v1 (current)
This version publication date	21 August 2025
First version publication date	21 August 2025

Trial information

Trial identification

Sponsor protocol code	54767414MMY3007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02195479
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to determine if the addition of daratumumab to VELCADE-melphalan-prednisone (VMP) would prolong progression-free survival (PFS) compared with VMP.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	98 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Czechia: 50
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 103
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Georgia: 22
Country: Number of subjects enrolled	Greece: 29
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Hungary: 26
Country: Number of subjects enrolled	Italy: 54
Country: Number of subjects enrolled	Japan: 50
Country: Number of subjects enrolled	Korea, Republic of: 41
Country: Number of subjects enrolled	North Macedonia: 11
Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	Russian Federation: 43
Country: Number of subjects enrolled	Serbia: 10

Country: Number of subjects enrolled	Türkiye: 15
Country: Number of subjects enrolled	Ukraine: 48
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Bulgaria: 23
Worldwide total number of subjects	706
EEA total number of subjects	411

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)	60
From 65 to 84 years	635
85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total of 706 participants were enrolled in the study, out of which 700 participants received study treatment and no participant completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Velcade, Melphalan and Prednisone (VMP)

Arm description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m^2) as subcutaneous (SC) injection, twice weekly (BIW) at Weeks (wks) 1, 2, 4 and 5 in Cycle (C) 1 followed by once weekly (QW) at Weeks 1, 2, 4 and 5 in Cycles 2 to 9, melphalan 9 mg/m^2 orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9. Each treatment cycle was of 6 weeks. After completion of treatment, participants entered follow-up (FU) phase and were not started on subsequent anti-myeloma therapy without confirmed disease progression (assessed by the International Myeloma Working Group [IMWG] criteria). After implementation of Amendment 7, post interim overall survival (OS) analysis, sponsor confirmation of disease progression was no longer required prior to initiation of subsequent anti-myeloma therapy, except for participants who progressed on VMP arm and requested subsequent therapy with daratumumab.

Arm type	Experimental
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	Velcade
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at Weeks 1, 2, 4 and 5 in Cycle 1 followed by QW at Weeks 1, 2, 4 and 5 in Cycles 2 to 9.

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

Dosage and administration details:

Participants received prednisone 60 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9.

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

Dosage and administration details:

Participants received melphalan 9 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9.

Arm title	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)

Arm description:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at wks 1, 2, 4 and 5 in C1 followed by QW at wks 1, 2, 4 and 5 in C2-9, melphalan 9 mg/m^2, orally QD on Days 1-4 and prednisone 60 mg/m^2, orally QD on Days 2-4 of each cycle up to C9. Participants also received daratumumab 16 milligrams per kilogram(mg/kg) as intravenous(IV) infusion QW for 6 wks in C1, Q3W in C2-9 and thereafter, Q4W (post-VMP phase) until PD, unacceptable toxicity, or study end. On Day 1 of each cycle, dexamethasone 20 mg IV or per oral was given 1 hour or less prior to daratumumab infusion as premedication and prednisone substitute. Each cycle was 6 wks. After Amendment 7, participants who were ongoing with daratumumab IV were given an option to switch to daratumumab SC injection on Day 1 of any cycle, per investigator's discretion. After completion of treatment, participants entered FU phase and were not started on subsequent anti-myeloma therapy without confirmed PD (assessed by IMWG criteria).

Arm type	Experimental
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	Velcade
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at Weeks 1, 2, 4 and 5 in Cycle 1 followed by QW at weeks 1, 2, 4 and 5 in Cycles 2 to 9.

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

Dosage and administration details:

Participants received melphalan 9 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9.

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

Dosage and administration details:

Participants received prednisone 60 mg/m^2 orally QD on Days 2 to 4 of each cycle up to Cycle 9.

Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received daratumumab 16 mg/kg as IV infusion QW for 6 weeks in Cycle 1 and then once every 3 weeks in Cycle 2 to 9 and thereafter, once every 4 weeks (post-VMP phase) until PD, unacceptable toxicity, or study end.

Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

After Amendment 7, participants who were ongoing with daratumumab IV treatment were given an option to switch to daratumumab SC injection on Day 1 of any cycle, at investigator's discretion, until PD, unacceptable toxicity, or study end.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

Participants received dexamethasone 20 mg IV 1 hour or less prior to daratumumab infusion as pre medication and prednisone substitute on Day 1 of each cycle.

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

Dosage and administration details:

Participants received dexamethasone 20 mg per oral 1 hour or less prior to daratumumab infusion as pre medication and prednisone substitute on Day 1 of each cycle.

Number of subjects in period 1	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)
Started	356	350
Treated	354	346
Completed	0	0
Not completed	356	350
Adverse event, serious fatal	217	171
Physician decision	1	-
Consent withdrawn by subject	30	30
Unspecified	3	4
Lost to follow-up	18	15
Discontinued at clinical cutoff	87	130

Baseline characteristics

Reporting groups	
Reporting group title	Velcade, Melphalan and Prednisone (VMP)

Reporting group description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m^2) as subcutaneous (SC) injection, twice weekly (BIW) at Weeks (wks) 1, 2, 4 and 5 in Cycle (C) 1 followed by once weekly (QW) at Weeks 1, 2, 4 and 5 in Cycles 2 to 9, melphalan 9 mg/m^2 orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9. Each treatment cycle was of 6 weeks. After completion of treatment, participants entered follow-up (FU) phase and were not started on subsequent anti-myeloma therapy without confirmed disease progression (assessed by the International Myeloma Working Group [IMWG] criteria). After implementation of Amendment 7, post interim overall survival (OS) analysis, sponsor confirmation of disease progression was no longer required prior to initiation of subsequent anti-myeloma therapy, except for participants who progressed on VMP arm and requested subsequent therapy with daratumumab.

Reporting group title	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)

Reporting group description:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at wks 1, 2, 4 and 5 in C1 followed by QW at wks 1, 2, 4 and 5 in C2-9, melphalan 9 mg/m^2, orally QD on Days 1-4 and prednisone 60 mg/m^2, orally QD on Days 2-4 of each cycle up to C9. Participants also received daratumumab 16 milligrams per kilogram(mg/kg) as intravenous(IV) infusion QW for 6 wks in C1, Q3W in C2-9 and thereafter, Q4W (post-VMP phase) until PD, unacceptable toxicity, or study end. On Day 1 of each cycle, dexamethasone 20 mg IV or per oral was given 1 hour or less prior to daratumumab infusion as premedication and prednisone substitute. Each cycle was 6 wks. After Amendment 7, participants who were ongoing with daratumumab IV were given an option to switch to daratumumab SC injection on Day 1 of any cycle, per investigator's discretion. After completion of treatment, participants entered FU phase and were not started on subsequent anti-myeloma therapy without confirmed PD (assessed by IMWG criteria).

Reporting group values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)	Total
Number of subjects	356	350	706
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional 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
12 - 17 years	0	0	0
Adults (18 - 64 years)	24	36	60
From 65 - 84 years	327	308	635
85 years and over	5	6	11
Age continuous Units: years			
arithmetic mean	71.5	71.3	
standard deviation	± 5.82	± 6.66	-
Gender categorical Units: Subjects			
Male	167	160	327
Female	189	190	379

Stage of Disease (ISS)			
The International Staging System (ISS) consists of following 3 stages - Stage I: serum beta2-microglobulin less than (<) 3.5 milligrams per liter (mg/L) and albumin greater than or equal to (>=) 3.5 grams per 100 Milliliter (g/100 mL); Stage II: neither stage I nor stage III and Stage III: serum beta2- microglobulin >= 5.5 mg/L.			
Units: Subjects			
Stage I	67	69	136
Stage II	160	139	299
Stage III	129	142	271
Time from multiple myeloma (MM) diagnosis			
Time from multiple myeloma (MM) diagnosis was the time from diagnosis of multiple myeloma to randomisation in each treatment group.			
Units: Months			
arithmetic mean	1.27	1.09	
standard deviation	± 1.737	± 1.056	-

End points

End points reporting groups

Reporting group title	Velcade, Melphalan and Prednisone (VMP)

Reporting group description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m^2) as subcutaneous (SC) injection, twice weekly (BIW) at Weeks (wks) 1, 2, 4 and 5 in Cycle (C) 1 followed by once weekly (QW) at Weeks 1, 2, 4 and 5 in Cycles 2 to 9, melphalan 9 mg/m^2 orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9. Each treatment cycle was of 6 weeks. After completion of treatment, participants entered follow-up (FU) phase and were not started on subsequent anti-myeloma therapy without confirmed disease progression (assessed by the International Myeloma Working Group [IMWG] criteria). After implementation of Amendment 7, post interim overall survival (OS) analysis, sponsor confirmation of disease progression was no longer required prior to initiation of subsequent anti-myeloma therapy, except for participants who progressed on VMP arm and requested subsequent therapy with daratumumab.

Reporting group title	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)

Reporting group description:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at wks 1, 2, 4 and 5 in C1 followed by QW at wks 1, 2, 4 and 5 in C2-9, melphalan 9 mg/m^2, orally QD on Days 1-4 and prednisone 60 mg/m^2, orally QD on Days 2-4 of each cycle up to C9. Participants also received daratumumab 16 milligrams per kilogram(mg/kg) as intravenous(IV) infusion QW for 6 wks in C1, Q3W in C2-9 and thereafter, Q4W (post-VMP phase) until PD, unacceptable toxicity, or study end. On Day 1 of each cycle, dexamethasone 20 mg IV or per oral was given 1 hour or less prior to daratumumab infusion as premedication and prednisone substitute. Each cycle was 6 wks. After Amendment 7, participants who were ongoing with daratumumab IV were given an option to switch to daratumumab SC injection on Day 1 of any cycle, per investigator's discretion. After completion of treatment, participants entered FU phase and were not started on subsequent anti-myeloma therapy without confirmed PD (assessed by IMWG criteria).

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[1]

End point description:

PFS: time from date of randomisation to PD/death. PD(IMWG)-Increase of 25% from lowest response value in any 1: Serum M-component (absolute increase >=0.5 grams per deciliter[g/dL]); Urine M-component (absolute increase >=200 milligrams[mg]/24 hours); Only participants without measurable serum and urine M-protein levels: difference between involved and uninvolved free light chain(FLC) levels(absolute increase>10mg/dL); Only participants without measurable serum and urine M-protein levels, without measurable disease by FLC levels, bone marrow Plasma cells(PC)% (absolute% >=10%);Bone marrow PC%: absolute% >10%; Definite development of new bone lesions/soft tissue plasmacytomas/definite increase in size of existing bone lesions/soft tissue plasmacytomas and Development of hypercalcemia (corrected serum calcium>11.5mg/dL) attributed solely to PC proliferative disorder. Intent-to-treat(ITT):all participants randomised. 99999:median/95% CI not estimable due to insufficient number of events.

End point type	Primary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

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: Only descriptive data was planned to be reported for this endpoint.

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	18.14 (16.53 to 19.91)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR: percentage of participants who achieved a partial response (PR) or better, according to IMWG criteria. IMWG criteria for PR: greater than or equal to (>=) 50 percentage (%) reduction of serum M-protein and reduction in 24 hour urinary M-protein by >=90% or to less than (<) 200 mg/24 hours, if serum and urine M-protein are not measurable, decrease of >=50% in difference between involved and uninvolved FLC levels was required in place of M-protein criteria, If serum and urine M-protein were not measurable, and serum free light assay was also not measurable, >=50% reduction in bone marrow plasma cells (PC) was required in place of M-protein, provided baseline bone marrow PC percentage was >=30%, in addition to above criteria, if present at baseline, a >=50% reduction in size of soft tissue plasmacytomas was also required. ITT set: all participants randomised into the study; classified according to assigned treatment group, regardless of actual the treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Percentage of participants				
number (not applicable)	73.9	90.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Very Good Partial Response (VGPR) or Better

End point title	Percentage of Participants With Very Good Partial Response

	(VGPR) or Better

End point description:

VGPR or better rate was defined as the percentage of participants who achieved VGPR or complete response (CR) (including stringent complete response [sCR]) according to the IMWG criteria during or after the study treatment. VGPR: Serum and urine component detectable by immunofixation but not on electrophoresis, or >=90% reduction in serum M-protein plus urine M-protein level <100 mg per 24 hour; CR: negative immunofixation on the serum and urine, Disappearance of any soft tissue plasmacytomas and <5% PC in bone marrow; sCR: CR in addition to having a normal FLC ratio and an absence of clonal cells in bone marrow by immunohistochemistry, immunofluorescence, 2-4 color flow cytometry. ITT set: all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Percentage of participants				
number (not applicable)	49.7	71.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Stringent Complete Response (sCR)

End point title	Percentage of Participants With Stringent Complete Response (sCR)

End point description:

sCR as per IMWG criteria was CR plus normal FLC ratio and absence of clonal PCs by immunohistochemistry, immunofluorescence or 2- to 4-color flow cytometry. CR: Negative immunofixation on the serum and urine; Disappearance of any soft tissue plasmacytomas; <5% PC in bone marrow. ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Percentage of participants				
number (not applicable)	7.0	18.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Complete Response (CR) or Better

End point title	Percentage of Participants With Complete Response (CR) or Better

End point description:

CR or better rate was defined as the percentage of participants with a CR or better (that is. CR and sCR) as per IMWG criteria. CR: as negative immunofixation on the serum and urine and disappearance of soft tissue plasmacytomas and <5 percent plasma cells in bone marrow; sCR: CR plus normal FLC ratio and absence of clonal PCs by immunohistochemistry, immunofluorescence or 2- to 4-color flow cytometry. ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Percentage of participants				
number (not applicable)	24.4	42.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Negative Minimal Residual Disease (MRD)

End point title	Percentage of Participants With Negative Minimal Residual Disease (MRD)

End point description:

The Minimal Residual Disease negativity rate was defined as the percentage of participants who had negative MRD (detection of less than 1 malignant cell among 100,000 normal cells) assessment at any

timepoint after the first dose of study drugs by evaluation of bone marrow aspirates or whole blood at 10^-5 threshold. MRD was evaluated by using Deoxyribonucleic acid (DNA) sequencing of immunoglobulin genes. MRD was assessed in participants who achieved complete response or stringent complete response (CR/sCR). ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 8.3 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Percentage of participants				
number (not applicable)	7.0	28.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival (OS) was measured from the date of randomisation to date of death. Median Overall Survival was estimated by using the Kaplan-Meier method. ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received. Here, '99999' signifies that upper limit of 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 8.3 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	53.59 (46.32 to 60.91)	82.96 (72.48 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression (TTP)

End point title	Time to Disease Progression (TTP)

End point description:

TTP: Time from date of randomisation to date of first documented evidence of confirmed PD or death due to PD, whichever occurs first. PD(IMWG)-Increase of 25% from lowest response value in any 1: Serum M-component (absolute increase >=0.5g/dL); Urine M-component (absolute increase >=200mg/24hours); Only in participants without measurable serum and urine M-protein levels: difference between involved and uninvolved FLC levels (absolute increase >10mg/dL); Only in participants without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow PC% (absolute% >=10%); Bone marrow PC%: absolute% >10%; Definite development of new bone lesions/soft tissue plasmacytomas or definite increase in size of existing bone lesions/soft tissue plasmacytomas and Development of hypercalcemia (corrected serum calcium>11.5mg/dL) that attributed solely to PC proliferative disorder. ITT set. 99999:median/95% CI was not estimable due to insufficient number of events.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	19.35 (17.38 to 22.67)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)

End point description:

TTR: time between date of randomisation and first efficacy evaluation that participant had met all criteria for PR or better. PR: >=50% reduction of serum and reduction in 24hour(h) urinary M-protein by >=90% or to <200mg/24h; If serum and urine M-protein were not measurable, decrease of >=50% in difference between involved and uninvolved FLC levels required in place of M-protein criteria; If serum and urine M-protein were not measurable and serum free light assay was also not measurable, >=50% reduction in bone marrow PCs required in place of M-protein, provided baseline bone marrow PC% >=30%; if present at baseline, >=50% reduction in size of soft tissue plasmacytomas required. Response-evaluable set (RES): participants who confirmed diagnosis of MM and measurable disease at baseline or screening, must receive at least 1 component of study treatment and adequate post-baseline disease assessments. N(overall number of participants analysed)=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	318		
Units: Months				
median (full range (min-max))	0.82 (0.7 to 12.6)	0.79 (0.4 to 15.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival on Next Line of Therapy (PFS2)

End point title	Progression Free Survival on Next Line of Therapy (PFS2)

End point description:

Progression-free survival after next-line therapy is defined as the time from randomisation to progression on the next line of subsequent antimyeloma therapy or death due to any cause (prior to start of second line of antimyeloma therapy), whichever comes first. Disease progression on next line of treatment was based on investigator judgment. ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 8.3 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	42.41 (37.29 to 47.05)	66.73 (58.58 to 80.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR: time between first documentation of response(confirmed PR/better) and date of PD or death due to PD. PD(IMWG criteria):PD increase of 25% from lowest response value in any: Serum M-component(absolute increase>=0.5g/dL);Urine M-component(absolute increase>=200mg/24h); Only participants without measurable serum and urine M-protein levels: difference between involved and uninvolved FLC levels (absolute increase>10mg/dL);Only participants without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow PC(absolute%>=10%);Bone marrow PC%:absolute%>10%;Definite development of new bone lesions/soft tissue plasmacytomas/definite increase in size of existing bone lesions/soft tissue plasmacytomas and Development of hypercalcemia(corrected serum calcium >11.5mg/dL) attributed to PC proliferative disorder. RES. N:participants evaluable for this endpoint. 99999:median and 95% CI not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first documentation of response up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	318		
Units: Months				
median (confidence interval 95%)	21.3 (18.4 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Treatment (TNT)

End point title	Time to Next Treatment (TNT)

End point description:

Time to next treatment was defined as the time from randomisation to the start of the next-line treatment. Kaplan-Meier method was used for the analysis. ITT set included all participants randomised into the study; classified according to assigned treatment group, regardless of the actual treatment received. Here, '99999' signifies that upper limit of 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From randomisation (Day -3) up to 8.3 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	25.9 (23.4 to 28.6)	66.8 (47.9 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Best M-protein Response

End point title	Percentage of Participants With Best M-protein Response

End point description:

Percentage of participants with Best M- protein response (BMpR) of 100% reduction and >=90% to <100% reduction were assessed. Best M-protein response was defined as the maximal percent reduction or the lowest percent increase from baseline in serum M-protein for participants with measurable heavy chain at baseline or urine M-protein for participants without measurable heavy chain, but with measurable light chain disease at baseline. For participants without measurable heavy chain and light chain disease at baseline, best response in serum free light chain (FLC) was defined as the maximal percent reduction or the lowest percent increase from baseline in the difference between involved and uninvolved serum FLC level (dFLC). Response-evaluable set was used. Here, 'n' (number analysed) signifies number of participants analysed for each specified category

End point type	Secondary

End point timeframe:

Up to 2.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	337		
Units: Percentage of participants				
number (not applicable)				
BMpR in serum: 100% reduction n= 287, 277	38.7	58.5		
BMpR in serum: >= 90 to < 100% n= 287, 277	14.6	15.2		
BMpR in urine: 100% reduction n=36,42	69.4	90.5		
BMpR in urine: >=90 to <100% n=36,42	13.9	7.1		
Best response(BR) in dFLC:100% reduction n=18, 18	0	0		
BR in dFLC: >=90% to <100% reduction n=18, 18	77.8	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30: Emotional Functioning Score

End point title	Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30: Emotional Functioning Score

End point description:

EORTC QLQ-C30: 30 items self-reporting questionnaire, with 1 week recall period, resulting in 5 functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning), 1 Global Health Status(GHS) scale, 3 symptom scales (fatigue, nausea and vomiting, pain), 6 single symptom items (dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties). Questionnaire had 28 items with 4-point Likert type responses (1=not at all; 4=very much) to assess functioning and symptoms; 2 items with 7-point Likert scales (1=poor; 7=excellent) for global health and overall QoL. Scores transformed to 0-100 scale, higher scores=better GHS, better functioning, more symptoms. Negative change from baseline values for function and GHS scale= deterioration in quality of life or functioning and positive values indicate improvement. ITT set used. N=participants evaluable for this endpoint; n=participants analysed at each specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day -24), Months 3, 6, 9, 12 ,18, 24, 30, 36, 42 and 48

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	317		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Month 3; n= 245,262	9.4 (7.1 to 11.6)	8.5 (6.3 to 10.7)		
Month 6; n= 213, 235	10.5 (8.1 to 12.9)	10.8 (8.6 to 13.1)		
Month 9; n= 189, 228	11.8 (9.4 to 14.3)	11.1 (8.8 to 13.4)		
Month 12; n= 185, 222	11.2 (8.7 to 13.7)	12.6 (10.3 to 14.9)		
Month 18; n= 136, 195	12.8 (10.1 to 15.6)	12.5 (10.1 to 14.9)		
Month 24; n= 83, 152	11.8 (8.5 to 15.1)	10.7 (8.2 to 13.3)		
Month 30; n= 71, 159	10.8 (7.3 to 14.3)	12.4 (9.8 to 14.9)		

Month 36; n=48, 145	10.8 (6.7 to 14.9)	12.3 (9.6 to 14.9)		
Month 42; n=33,125	6.5 (1.7 to 11.4)	12.8 (10 to 15.6)		
Month 48; n=23,102	6.2 (0.5 to 11.9)	10.5 (7.5 to 13.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30: Global Health Scale

End point title	Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30: Global Health Scale

End point description:

EORTC QLQ-C30: 30 items self-reporting questionnaire, with 1 week recall period, resulting in 5 functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), 1 GHS scale, 3 symptom scales (fatigue, nausea and vomiting, and pain), and 6 single symptom items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Questionnaire had 28 items with 4-point Likert type responses (1=not at all; 4=very much) to assess functioning and symptoms; 2 items with 7-point Likert scales (1=poor; 7=excellent) for global health and overall QoL. Scores were transformed to 0-100 scale, higher scores=better GHS, better functioning, more symptoms. Negative change from baseline values for function and GHS scale=deterioration in quality of life or functioning and positive values indicate improvement. ITT used. N=participants evaluable for this endpoint; n=participants analysed at each specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day -24), Months 3, 6, 9, 12 ,18, 24, 30, 36, 42 and 48

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	317		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Month 3; n=245, 262	4 (1.7 to 6.3)	7.5 (5.2 to 9.7)		
Month 6; n=213, 235	8.8 (6.4 to 11.3)	8.5 (6.2 to 10.8)		
Month 9; n=189, 228	10.2 (7.7 to 12.8)	10.6 (8.2 to 12.9)		
Month 12; n=185, 222	10.7 (8.2 to 13.3)	11.4 (9 to 13.7)		
Month 18; n=136, 195	11.8 (9 to 14.6)	12.8 (10.3 to 15.3)		
Month 24; n=83, 152	11.5 (8.1 to 15)	9.5 (6.8 to 12.1)		

Month 30; n=71, 159	10.8 (7.1 to 14.5)	11.8 (9.2 to 14.5)		
Month 36; n=48, 145	8.6 (4.2 to 12.9)	11.9 (9.1 to 14.6)		
Month 42; n=33, 125	4.8 (-0.3 to 9.9)	10.4 (7.5 to 13.3)		
Month 48; n=23, 102	8.9 (2.8 to 14.9)	9.8 (6.6 to 12.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol-5 Dimensions-5 Levels (EQ-5D-5L): Visual Analogue Scale (VAS)

End point title	Change From Baseline in EuroQol-5 Dimensions-5 Levels (EQ-5D-5L): Visual Analogue Scale (VAS)

End point description:

EQ-5D-5L was a standardized, participant-rated questionnaire to assess health-related quality of life. The EQ-5D-5L included 2 components: the EQ-5D-5L health state profile (descriptive system) and the EQ-5D-5L Visual Analog Scale. The Visual Analogue Scale was designed to rate the participant's current health state on a scale from 0 to 100, where 0 represents the worst imaginable health state and 100 represents the best imaginable health state. ITT set: participants randomised into the study; classified according to assigned treatment group, regardless actual treatment received. 'N' (overall number of participants analysed) signifies participants evaluable for this endpoint; 'n' (number analysed) signifies number of participants who were analysed at each specified timepoint, for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Day -24), Months 3, 6, 9, 12 ,18, 24, 30, 36, 42 and 48

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	315		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Month 3; n= 242, 258	4.27 (± 18.38)	9.37 (± 20.222)		
Month 6; n=210, 230	7.51 (± 17.957)	11.02 (± 20.168)		
Month 9; n=185, 227	10.08 (± 19.475)	12.51 (± 20.564)		
Month 12; n=185, 217	11.1 (± 19.139)	10.93 (± 20.447)		
Month 18; n=134, 194	10.75 (± 21.146)	15.35 (± 21.168)		
Month 24; n=82, 150	10.62 (± 19.531)	12.17 (± 22.592)		
Month 30; n=71, 157	12.38 (± 21.817)	14.41 (± 21.305)		

Month 36; n=46, 143	12 (± 23.856)	13.94 (± 21.984)		
Month 42; n=33, 123	12.88 (± 23.789)	14.33 (± 21.502)		
Month 48; n=23, 99	9.17 (± 18.612)	11.93 (± 24.031)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol 5 Dimensions-5 Level (EQ-5D-5L) Utility Score

End point title	Change From Baseline in EuroQol 5 Dimensions-5 Level (EQ-5D-5L) Utility Score

End point description:

EQ-5D-5L included health state profile (descriptive system) and VAS. EQ-5D-5L descriptive system provided profile of participant's health state 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Each dimension had 5 response (no problems, slight problems, moderate problems, severe problems and extreme problems) reflected increasing levels of difficulty. Participant was asked for current health state by selecting most appropriate level in each of 5 dimensions. Responses to 5 dimension scores were combined and converted into single preference-weighted health utility index score 0(worst health state) to 1(better health state) representing GHS of individual based on UK scoring algorithm. ITT set. N=participants evaluable for this endpoint; n=number of participants who were analysed at each specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day -24), Months 3, 6, 9, 12 ,18, 24, 30, 36, 42 and 48

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	315		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Month 3; n= 242, 258	0.09 (± 0.312)	0.12 (± 0.266)		
Month 6; n= 210, 230	0.12 (± 0.269)	0.14 (± 0.271)		
Month 9; n= 185, 227	0.16 (± 0.27)	0.16 (± 0.271)		
Month 12; n= 185, 217	0.15 (± 0.281)	0.17 (± 0.288)		
Month 18; n= 134, 194	0.14 (± 0.268)	0.17 (± 0.293)		
Month 24; n= 82, 150	0.15 (± 0.252)	0.18 (± 0.312)		
Month 30; n= 71, 157	0.16 (± 0.291)	0.19 (± 0.303)		
Month 36; n= 47, 143	0.16 (± 0.315)	0.21 (± 0.306)		
Month 42; n= 33, 123	0.08 (± 0.303)	0.2 (± 0.287)		
Month 48; n= 23, 99	0.07 (± 0.246)	0.15 (± 0.319)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Progression Free Survival at Data Cutoff Date of 24 June 2019

End point title	Progression Free Survival at Data Cutoff Date of 24 June 2019

End point description:

PFS- duration from date of randomisation to PD/death, whichever occurs first. PD per IMWG criteria- Increase of 25% from lowest response value in 1 of following: Serum M-component (absolute increase >=0.5 g/dL); Urine M-component (absolute increase >=200 mg/24 hours); Only participants without measurable serum and urine M-protein levels: difference between involved and uninvolved FLC levels (absolute increase >10 mg/dL); Only participants without measurable serum and urine M-protein levels, without measurable disease by FLC levels, bone marrow PC % (absolute % >=10%); Bone marrow PC %: absolute % >10%; Definite development of new bone lesions/soft tissue plasmacytomas/definite increase in size of existing bone lesions/soft tissue plasmacytomas and development of hypercalcemia (corrected serum calcium [CSC] >11.5 mg/dL) that can be attributed solely to the PC proliferative disorder. ITT set was used.

End point type	Post-hoc

End point timeframe:

From randomisation (Day -3) up to 4.4 years

End point values	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	350		
Units: Months				
median (confidence interval 95%)	19.29 (17.97 to 20.40)	36.40 (32.13 to 45.90)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Day 1) up to 30 days after last dose of study treatment (up to 8.2 years)

Adverse event reporting additional description:

Safety population defined as participants who had received at least 1 administration of any study treatment (partial or complete) and were analyzed according to treatment actually received. In this study, 'occurrences causally related to treatment' represented the occurrences related to daratumumab treatment only.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Velcade, Melphalan and Prednisone (VMP)

Reporting group description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m^2) as subcutaneous (SC) injection, twice weekly (BIW) at Weeks (wks) 1, 2, 4 and 5 in Cycle (C) 1 followed by once weekly (QW) at Weeks 1, 2, 4 and 5 in Cycles 2 to 9, melphalan 9 mg/m^2 orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m^2 orally QD on Days 1 to 4 of each cycle up to Cycle 9. Each treatment cycle was of 6 weeks. After completion of treatment, participants entered follow-up (FU) phase and were not started on subsequent anti-myeloma therapy without confirmed disease progression (assessed by the International Myeloma Working Group [IMWG] criteria). After implementation of Amendment 7, post interim overall survival (OS) analysis, sponsor confirmation of disease progression was no longer required prior to initiation of subsequent anti-myeloma therapy, except for participants who progressed on VMP arm and requested subsequent therapy with daratumumab.

Reporting group title	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)

Reporting group description:

Participants received Velcade 1.3 mg/m^2 as SC injection, BIW at wks 1, 2, 4 and 5 in C1 followed by QW at wks 1, 2, 4 and 5 in C2-9, melphalan 9 mg/m^2, orally QD on Days 1-4 and prednisone 60 mg/m^2, orally QD on Days 2-4 of each cycle up to C9. Participants also received daratumumab 16 milligrams per kilogram(mg/kg) as intravenous(IV) infusion QW for 6 wks in C1, Q3W in C2-9 and thereafter, Q4W (post-VMP phase) until PD, unacceptable toxicity, or study end. On Day 1 of each cycle, dexamethasone 20 mg IV or per oral was given 1 hour or less prior to daratumumab infusion as premedication and prednisone substitute. Each cycle was 6 wks. After Amendment 7, participants who were ongoing with daratumumab IV were given an option to switch to daratumumab SC injection on Day 1 of any cycle, per investigator’s discretion. After completion of treatment, participants entered FU phase and were not started on subsequent anti-myeloma therapy without confirmed PD (assessed by IMWG criteria).

Serious adverse events	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)	
Total subjects affected by serious adverse events			
subjects affected / exposed	117 / 354 (33.05%)	186 / 346 (53.76%)	
number of deaths (all causes)	217	172	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal Adenocarcinoma			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile Duct Cancer			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma of Colon			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute Myeloid Leukaemia			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic Cancer			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant Melanoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine Tumour			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oesophageal Adenocarcinoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma of Lung			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cell Carcinoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Adenocarcinoma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic Adenoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Crisis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Hypotension			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic Shock			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Pain			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			

subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Fatigue			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised Oedema			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 354 (1.41%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated Hernia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-Cardiac Chest Pain			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute Respiratory Failure			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	9 / 10	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bronchiectasis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial Lung Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal Oedema			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive Airways Disorder			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural Effusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Aspiration			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchospasm			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	4 / 354 (1.13%)	7 / 346 (2.02%)	
occurrences causally related to treatment / all	0 / 4	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea Exertional			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax Spontaneous			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	4 / 354 (1.13%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary Oedema			
subjects affected / exposed	0 / 354 (0.00%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 0	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachypnoea			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic Disorder			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Delirium			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Troponin Increased			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen Saturation Decreased			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-Reactive Protein Increased			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Creatinine Increased			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate Aminotransferase Increased			

subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Neck Fracture			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist Fracture			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	2 / 354 (0.56%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Shock			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Toxicity to Various Agents			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Laceration			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic Bone Injury			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion Related Reaction			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Limb Fracture			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic Cardiomyopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Left Ventricular Failure			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute Myocardial Infarction			
subjects affected / exposed	0 / 354 (0.00%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 0	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute Coronary Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Unstable			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular Block Second Degree			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrest			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Myocardial Infarction			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure Acute			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac Failure Chronic			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-Respiratory Arrest			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular Insufficiency			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac Failure			
subjects affected / exposed	8 / 354 (2.26%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 8	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sinus Bradycardia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress Cardiomyopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus Node Dysfunction			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhage Intracranial			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Ischaemia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Infarction			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Autonomic Nervous System Imbalance			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurotoxicity			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Parkinson's Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral Motor Neuropathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Cord Compression			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Sensorimotor Neuropathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Sensory Neuropathy			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	7 / 354 (1.98%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	9 / 354 (2.54%)	8 / 346 (2.31%)	
occurrences causally related to treatment / all	0 / 12	6 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 354 (1.13%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	0 / 5	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	4 / 354 (1.13%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 4	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctival Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Detachment			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendiceal Mucocoele			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Adhesions			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Wall Haematoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Abdomen			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular Perforation			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Hernia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Dilatation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Disorder			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Rupture			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis Haemorrhagic			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Polyp			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	6 / 354 (1.69%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus Paralytic			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash Vesicular			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash Erythematous			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema Multiforme			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus Ulcer			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	5 / 354 (1.41%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prerenal Failure			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal Failure			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Retention			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Kidney Disease			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Dactylitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Pain			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			

subjects affected / exposed	3 / 354 (0.85%)	7 / 346 (2.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Stenosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Pain			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck Pain			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal Pain			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium Difficile Infection			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Abscess			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical Pneumonia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 354 (0.56%)	10 / 346 (2.89%)	
occurrences causally related to treatment / all	0 / 2	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida Sepsis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Colitis			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Colitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	0 / 354 (0.00%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 2	
Infective Myositis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus Infection Reactivation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal Bacteraemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Bacteraemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1n1 Influenza			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster Disseminated			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Fistula			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infection			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective Exacerbation of Chronic Obstructive Airways Disease			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19 Pneumonia			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 354 (0.56%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Sepsis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Pneumococcal			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic Infection			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic Infection			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pharyngitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal Sepsis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	13 / 354 (3.67%)	53 / 346 (15.32%)	
occurrences causally related to treatment / all	2 / 16	14 / 61	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia Pneumococcal			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Streptococcal			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Viral			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Abscess			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous Colitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection			
subjects affected / exposed	3 / 354 (0.85%)	10 / 346 (2.89%)	
occurrences causally related to treatment / all	0 / 3	4 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis Acute			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	5 / 354 (1.41%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 8	2 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic Shock			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Staphylococcal Infection			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous Pleurisy			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 354 (1.13%)	7 / 346 (2.02%)	
occurrences causally related to treatment / all	1 / 5	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary Tract Infection			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular Device Infection			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Tumour Lysis Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hypophagia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased Appetite			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Velcade, Melphalan and Prednisone (VMP)	Daratumumab, Velcade, Melphalan and Prednisone (D-VMP)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	338 / 354 (95.48%)	333 / 346 (96.24%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Adenocarcinoma of Colon			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Adenoma Benign			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Basal Cell Carcinoma			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences (all)	4	6	
Benign Breast Neoplasm			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Benign Lung Neoplasm			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Bladder Neoplasm			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Bowen's Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Carcinoma in Situ			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Colon Adenoma			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Essential Thrombocythaemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Eye Naevus			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gastrointestinal Tract Adenoma			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Lipoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Melanocytic Naevus			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Plasma Cell Leukaemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Seborrhoeic Keratosis			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Skin Papilloma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Uterine Leiomyoma			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	

Aortic Arteriosclerosis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Aortic Stenosis			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	6	
Arteriosclerosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Deep Vein Thrombosis			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Embolism			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	2 / 354 (0.56%)	4 / 346 (1.16%)	
occurrences (all)	2	4	
Haematoma			
subjects affected / exposed	6 / 354 (1.69%)	6 / 346 (1.73%)	
occurrences (all)	6	7	
Hot Flush			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Hyperaemia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Hypertension			
subjects affected / exposed	10 / 354 (2.82%)	50 / 346 (14.45%)	
occurrences (all)	12	88	
Hypertensive Crisis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Hypotension			
subjects affected / exposed	23 / 354 (6.50%)	32 / 346 (9.25%)	
occurrences (all)	25	35	

Lymphoedema			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Microangiopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Orthostatic Hypotension			
subjects affected / exposed	3 / 354 (0.85%)	6 / 346 (1.73%)	
occurrences (all)	3	6	
Pallor			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Peripheral Artery Aneurysm			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Peripheral Coldness			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	4	
Thrombophlebitis			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Varicophlebitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Varicose Vein			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Vasculitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Venous Thrombosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Venous Thrombosis Limb			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Transurethral Prostatectomy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	43 / 354 (12.15%)	51 / 346 (14.74%)	
occurrences (all)	72	95	
Catheter Site Pain			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Catheter Site Phlebitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Chest Discomfort			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	4	
Chest Pain			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Chills			
subjects affected / exposed	6 / 354 (1.69%)	28 / 346 (8.09%)	
occurrences (all)	8	32	
Crepitations			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Discomfort			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	2	
Extravasation			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Face Oedema			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	3	4	
Fatigue			
subjects affected / exposed	50 / 354 (14.12%)	60 / 346 (17.34%)	
occurrences (all)	74	81	
Feeling Abnormal			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Gait Disturbance			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences (all)	2	8	
General Physical Health Deterioration			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Generalised Oedema			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Hyperthermia			
subjects affected / exposed	2 / 354 (0.56%)	7 / 346 (2.02%)	
occurrences (all)	2	11	
Inflammation			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Influenza Like Illness			
subjects affected / exposed	5 / 354 (1.41%)	18 / 346 (5.20%)	
occurrences (all)	9	26	
Infusion Site Erythema			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Infusion Site Extravasation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Infusion Site Pain			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Injection Site Bruising			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Injection Site Erythema			
subjects affected / exposed	28 / 354 (7.91%)	12 / 346 (3.47%)	
occurrences (all)	52	14	
Injection Site Haematoma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Injection Site Hypersensitivity			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Injection Site Induration			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Injection Site Pain			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Injection Site Pruritus			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Injection Site Rash			
subjects affected / exposed	3 / 354 (0.85%)	2 / 346 (0.58%)	
occurrences (all)	3	2	
Injection Site Swelling			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	10 / 354 (2.82%)	9 / 346 (2.60%)	
occurrences (all)	41	11	
Mass			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Non-Cardiac Chest Pain			

subjects affected / exposed	4 / 354 (1.13%)	13 / 346 (3.76%)	
occurrences (all)	5	15	
Oedema Peripheral			
subjects affected / exposed	39 / 354 (11.02%)	68 / 346 (19.65%)	
occurrences (all)	57	106	
Pain			
subjects affected / exposed	3 / 354 (0.85%)	4 / 346 (1.16%)	
occurrences (all)	3	4	
Peripheral Swelling			
subjects affected / exposed	9 / 354 (2.54%)	12 / 346 (3.47%)	
occurrences (all)	10	15	
Polyserositis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	70 / 354 (19.77%)	87 / 346 (25.14%)	
occurrences (all)	106	152	
Soft Tissue Inflammation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Temperature Intolerance			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Immune system disorders			
Allergy to Arthropod Bite			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Drug Hypersensitivity			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Hypersensitivity			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	

Seasonal Allergy			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Secondary Immunodeficiency			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Benign Prostatic Hyperplasia			
subjects affected / exposed	2 / 354 (0.56%)	7 / 346 (2.02%)	
occurrences (all)	2	7	
Breast Cyst			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Breast Mass			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Breast Pain			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Cystocele			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gynaecomastia			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Metrorrhagia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Ovarian Cyst			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Pelvic Pain			

subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Prostatic Fibrosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Prostatic Obstruction			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Prostatomegaly			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rectocele			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Testicular Pain			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Uterine Prolapse			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Vaginal Discharge			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Vaginal Haemorrhage			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Vulvovaginal Pruritus			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	1		
Aphonia				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Asthma				
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	1		
Atelectasis				
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	1		
Bronchiectasis				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Bronchospasm				
subjects affected / exposed	1 / 354 (0.28%)	11 / 346 (3.18%)		
occurrences (all)	3	11		
Catarrh				
subjects affected / exposed	2 / 354 (0.56%)	9 / 346 (2.60%)		
occurrences (all)	2	23		
Choking				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Chronic Obstructive Pulmonary Disease				
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)		
occurrences (all)	0	4		
Cough				
subjects affected / exposed	27 / 354 (7.63%)	70 / 346 (20.23%)		
occurrences (all)	32	105		
Dry Throat				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Dysphonia				
subjects affected / exposed	4 / 354 (1.13%)	5 / 346 (1.45%)		
occurrences (all)	4	5		

Dyspnoea			
subjects affected / exposed	14 / 354 (3.95%)	43 / 346 (12.43%)	
occurrences (all)	15	57	
Dyspnoea Exertional			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	4	
Dyspnoea at Rest			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	7 / 354 (1.98%)	9 / 346 (2.60%)	
occurrences (all)	7	11	
Haemoptysis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Hydrothorax			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Interstitial Lung Disease			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	3	
Laryngospasm			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Nasal Congestion			
subjects affected / exposed	0 / 354 (0.00%)	9 / 346 (2.60%)	
occurrences (all)	0	9	
Nasal Septum Haematoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Obstructive Airways Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

Oropharyngeal Discomfort			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Oropharyngeal Pain			
subjects affected / exposed	5 / 354 (1.41%)	14 / 346 (4.05%)	
occurrences (all)	5	20	
Orthopnoea			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Paranasal Cyst			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pharyngeal Paraesthesia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pleural Effusion			
subjects affected / exposed	1 / 354 (0.28%)	7 / 346 (2.02%)	
occurrences (all)	1	7	
Pleural Thickening			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pleurisy			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Pneumonia Aspiration			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pneumonitis			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Productive Cough			
subjects affected / exposed	5 / 354 (1.41%)	12 / 346 (3.47%)	
occurrences (all)	8	18	
Pulmonary Congestion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

Pulmonary Embolism			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pulmonary Fibrosis			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Pulmonary Mass			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Pulmonary Oedema			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Respiratory Acidosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Respiratory Alkalosis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Respiratory Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Respiratory Failure			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Respiratory Tract Inflammation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rhinitis Allergic			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Rhinorrhoea			
subjects affected / exposed	1 / 354 (0.28%)	8 / 346 (2.31%)	
occurrences (all)	1	10	
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Sneezing			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Sputum Increased			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Tachypnoea			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Throat Irritation			
subjects affected / exposed	0 / 354 (0.00%)	8 / 346 (2.31%)	
occurrences (all)	0	9	
Throat Tightness			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Upper Respiratory Tract Inflammation			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	5	
Upper Respiratory Tract Irritation			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Vasomotor Rhinitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Wheezing			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	1	5	
Psychiatric disorders			
Adjustment Disorder with Depressed Mood			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Agitation			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	9	
Anxiety			

subjects affected / exposed	8 / 354 (2.26%)	10 / 346 (2.89%)	
occurrences (all)	8	10	
Anxiety Disorder			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Bradyphrenia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Confusional State			
subjects affected / exposed	2 / 354 (0.56%)	7 / 346 (2.02%)	
occurrences (all)	2	7	
Delirium			
subjects affected / exposed	5 / 354 (1.41%)	5 / 346 (1.45%)	
occurrences (all)	7	7	
Depressed Mood			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	15 / 354 (4.24%)	12 / 346 (3.47%)	
occurrences (all)	17	12	
Disorientation			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Enuresis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Euphoric Mood			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	32 / 354 (9.04%)	33 / 346 (9.54%)	
occurrences (all)	36	47	
Mental Status Changes			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Mood Altered			

subjects affected / exposed	3 / 354 (0.85%)	3 / 346 (0.87%)	
occurrences (all)	3	3	
Mood Swings			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Nervousness			
subjects affected / exposed	2 / 354 (0.56%)	4 / 346 (1.16%)	
occurrences (all)	2	5	
Psychiatric Decompensation			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Restlessness			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Sleep Disorder			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Somatic Symptom Disorder			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Substance-Induced Psychotic Disorder			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Tension			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Product issues			
Device Occlusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Cholecystitis Chronic			

subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Cholelithiasis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Cholestasis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hepatic Function Abnormal			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Hepatic Steatosis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Hepatitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hepatitis Toxic			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Hepatosplenomegaly			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences (all)	4	11	
Liver Disorder			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Steatohepatitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Investigations			
Activated Partial Thromboplastin Time Prolonged			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Alanine Aminotransferase Increased			
subjects affected / exposed	17 / 354 (4.80%)	23 / 346 (6.65%)	
occurrences (all)	27	26	
Aspartate Aminotransferase Increased			
subjects affected / exposed	13 / 354 (3.67%)	19 / 346 (5.49%)	
occurrences (all)	21	23	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	10 / 354 (2.82%)	9 / 346 (2.60%)	
occurrences (all)	22	15	
Blood Calcium Increased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Blood Creatinine Increased			
subjects affected / exposed	17 / 354 (4.80%)	14 / 346 (4.05%)	
occurrences (all)	30	19	
Blood Iron Decreased			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	2	
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	3	3	
Blood Parathyroid Hormone Increased			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Blood Pressure Increased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Blood Urea Increased			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Breath Sounds Abnormal			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
C-Reactive Protein Increased			
subjects affected / exposed	10 / 354 (2.82%)	5 / 346 (1.45%)	
occurrences (all)	12	6	
Coagulation Time Shortened			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Creatinine Renal Clearance Decreased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ejection Fraction Decreased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Electrocardiogram Q Wave Abnormal			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram T Wave Inversion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Fibrin D Dimer Increased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	8 / 354 (2.26%)	13 / 346 (3.76%)	
occurrences (all)	14	25	
Globulins Decreased			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Immunoglobulins Decreased			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)		
occurrences (all)	0	2		
International Normalised Ratio Increased				
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)		
occurrences (all)	1	3		
Light Chain Analysis Increased				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	2		
Mean Cell Volume Increased				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Oxygen Saturation Decreased				
subjects affected / exposed	0 / 354 (0.00%)	6 / 346 (1.73%)		
occurrences (all)	0	6		
Platelet Count Increased				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Prothrombin Time Prolonged				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Serum Ferritin Decreased				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Serum Ferritin Increased				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Troponin Increased				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Vital Capacity Decreased				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Weight Decreased				
subjects affected / exposed	13 / 354 (3.67%)	14 / 346 (4.05%)		
occurrences (all)	14	15		

Weight Increased			
subjects affected / exposed	1 / 354 (0.28%)	6 / 346 (1.73%)	
occurrences (all)	1	11	
Injury, poisoning and procedural complications			
Anaemia Postoperative			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ankle Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Arthropod Bite			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Bone Contusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Clavicle Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Compression Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Concussion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	2 / 354 (0.56%)	15 / 346 (4.34%)	
occurrences (all)	2	17	
Craniocerebral Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ear Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Eye Contusion			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Eye Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Face Injury			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Fall			
subjects affected / exposed	8 / 354 (2.26%)	14 / 346 (4.05%)	
occurrences (all)	8	19	
Fibula Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Foot Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Forearm Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Fractured Sacrum			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Head Injury			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	4	
Humerus Fracture			
subjects affected / exposed	3 / 354 (0.85%)	2 / 346 (0.58%)	
occurrences (all)	3	2	
Ilium Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Joint Dislocation			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Joint Injury			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ligament Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ligament Sprain			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Limb Injury			
subjects affected / exposed	3 / 354 (0.85%)	6 / 346 (1.73%)	
occurrences (all)	3	7	
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Multiple Injuries			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Muscle Injury			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Overdose			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Pelvic Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Periorbital Haematoma			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Poisoning			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Post Procedural Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Post Procedural Oedema			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Procedural Pain			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Rib Fracture			
subjects affected / exposed	4 / 354 (1.13%)	4 / 346 (1.16%)	
occurrences (all)	4	5	
Skin Abrasion			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Skin Injury			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Skin Laceration			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Spinal Column Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Spinal Compression Fracture			
subjects affected / exposed	2 / 354 (0.56%)	7 / 346 (2.02%)	
occurrences (all)	3	8	
Spinal Fracture			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Subcutaneous Haematoma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Thermal Burn			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Tooth Fracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Transfusion Reaction			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Traumatic Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Upper Limb Fracture			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Wound			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Wound Dehiscence			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Wound Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Wrist Fracture			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hypertrophic Cardiomyopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	4 / 354 (1.13%)	6 / 346 (1.73%)	
occurrences (all)	4	8	
Aortic Valve Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Aortic Valve Incompetence			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Arrhythmia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	6	
Arrhythmia Supraventricular			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Atrial Fibrillation			
subjects affected / exposed	7 / 354 (1.98%)	20 / 346 (5.78%)	
occurrences (all)	7	26	
Atrial Flutter			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Atrioventricular Block			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Atrioventricular Block First Degree			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Bundle Branch Block Left			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Cardiac Arrest			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Cardiac Asthma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Cardiac Failure			
subjects affected / exposed	1 / 354 (0.28%)	6 / 346 (1.73%)	
occurrences (all)	1	7	
Cardiac Failure Chronic			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Cardiac Failure Congestive			

subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Cardiomyopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Coronary Artery Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Coronary Artery Occlusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Degenerative Mitral Valve Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Left Ventricular Failure			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Mitral Valve Disease			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Myocardial Ischaemia			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Palpitations			
subjects affected / exposed	6 / 354 (1.69%)	4 / 346 (1.16%)	
occurrences (all)	8	5	
Right Ventricular Failure			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Sinus Bradycardia			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Sinus Tachycardia			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	1	5	
Supraventricular Extrasystoles			

subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	8	5	
Tachycardia Paroxysmal			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Ventricular Arrhythmia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Ventricular Extrasystoles			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Ventricular Tachycardia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Altered State of Consciousness			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Amnesia			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Anosmia			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Aphasia			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Ataxia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Autonomic Nervous System Imbalance				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	2	0		
Axonal Neuropathy				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	2		
Balance Disorder				
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)		
occurrences (all)	1	2		
Carpal Tunnel Syndrome				
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	1		
Central Pain Syndrome				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Cerebral Haemorrhage				
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)		
occurrences (all)	1	0		
Cerebral Infarction				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Cerebrovascular Disorder				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Cognitive Disorder				
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)		
occurrences (all)	1	4		
Dementia Alzheimer's Type				
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)		
occurrences (all)	0	2		
Dementia with Lewy Bodies				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Depressed Level of Consciousness				

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Diabetic Neuropathy			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Disturbance in Attention			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	21 / 354 (5.93%)	33 / 346 (9.54%)	
occurrences (all)	26	58	
Dizziness Exertional			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Dizziness Postural			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Drooling			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Dysaesthesia			
subjects affected / exposed	3 / 354 (0.85%)	3 / 346 (0.87%)	
occurrences (all)	3	3	
Dysarthria			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Dysgeusia			
subjects affected / exposed	6 / 354 (1.69%)	8 / 346 (2.31%)	
occurrences (all)	10	9	
Dystonia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Facial Paralysis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Facial Paresis			

subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	12 / 354 (3.39%)	35 / 346 (10.12%)	
occurrences (all)	12	46	
Hemianaesthesia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Hyperaesthesia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	8 / 354 (2.26%)	5 / 346 (1.45%)	
occurrences (all)	15	8	
Hyposmia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Intercostal Neuralgia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ischaemic Stroke			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Lethargy			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Leukoencephalopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Loss of Consciousness			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Lumbosacral Plexopathy			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Lumbosacral Radiculopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Memory Impairment			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Migraine			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Movement Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Myelopathy			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Neuralgia			
subjects affected / exposed	16 / 354 (4.52%)	26 / 346 (7.51%)	
occurrences (all)	23	39	
Neuropathy Peripheral			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	3	3	
Optic Neuritis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Orthostatic Intolerance			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	19 / 354 (5.37%)	23 / 346 (6.65%)	
occurrences (all)	22	40	
Peripheral Motor Neuropathy			
subjects affected / exposed	4 / 354 (1.13%)	3 / 346 (0.87%)	
occurrences (all)	4	4	
Peripheral Sensorimotor Neuropathy			

subjects affected / exposed	8 / 354 (2.26%)	9 / 346 (2.60%)	
occurrences (all)	16	15	
Peripheral Sensory Neuropathy			
subjects affected / exposed	122 / 354 (34.46%)	100 / 346 (28.90%)	
occurrences (all)	212	192	
Peroneal Nerve Palsy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Piriformis Syndrome			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Poor Quality Sleep			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Post Herpetic Neuralgia			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	5	
Presyncope			
subjects affected / exposed	2 / 354 (0.56%)	5 / 346 (1.45%)	
occurrences (all)	5	7	
Psychomotor Hyperactivity			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Radiculopathy			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Restless Legs Syndrome			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Sciatica			
subjects affected / exposed	1 / 354 (0.28%)	8 / 346 (2.31%)	
occurrences (all)	1	9	
Seizure			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Slow Speech			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	4	
Syncope			
subjects affected / exposed	2 / 354 (0.56%)	10 / 346 (2.89%)	
occurrences (all)	5	13	
Taste Disorder			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Transient Ischaemic Attack			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Tremor			
subjects affected / exposed	5 / 354 (1.41%)	10 / 346 (2.89%)	
occurrences (all)	5	11	
Trigeminal Neuralgia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Visual Field Defect			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	129 / 354 (36.44%)	110 / 346 (31.79%)	
occurrences (all)	285	290	
Anaemia Vitamin B12 Deficiency			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Bone Marrow Failure			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Coagulopathy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

Disseminated Intravascular Coagulation				
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)		
occurrences (all)	0	2		
Eosinophilia				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	2		
Febrile Neutropenia				
subjects affected / exposed	3 / 354 (0.85%)	4 / 346 (1.16%)		
occurrences (all)	3	4		
Granulocytopenia				
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	4		
Haemolysis				
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)		
occurrences (all)	1	2		
Iron Deficiency Anaemia				
subjects affected / exposed	1 / 354 (0.28%)	10 / 346 (2.89%)		
occurrences (all)	2	17		
Leukocytosis				
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)		
occurrences (all)	1	1		
Leukopenia				
subjects affected / exposed	53 / 354 (14.97%)	47 / 346 (13.58%)		
occurrences (all)	222	300		
Lymphadenopathy				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Lymphocytosis				
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)		
occurrences (all)	2	0		
Lymphopenia				
subjects affected / exposed	36 / 354 (10.17%)	39 / 346 (11.27%)		
occurrences (all)	167	213		
Nephrogenic Anaemia				

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	186 / 354 (52.54%)	174 / 346 (50.29%)	
occurrences (all)	680	723	
Neutrophilia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	189 / 354 (53.39%)	172 / 346 (49.71%)	
occurrences (all)	720	707	
Thrombocytosis			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Deafness			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	2	3	
Deafness Neurosensory			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	4	
Deafness Unilateral			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Ear Congestion			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Ear Discomfort			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ear Pain			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	

Tinnitus			
subjects affected / exposed	2 / 354 (0.56%)	4 / 346 (1.16%)	
occurrences (all)	2	4	
Vertigo			
subjects affected / exposed	6 / 354 (1.69%)	9 / 346 (2.60%)	
occurrences (all)	10	12	
Eye disorders			
Asthenopia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Blepharitis			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	5	
Blindness			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Cataract			
subjects affected / exposed	4 / 354 (1.13%)	17 / 346 (4.91%)	
occurrences (all)	4	18	
Chalazion			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Conjunctival Cyst			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Conjunctival Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Conjunctivitis Allergic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Diabetic Retinopathy			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Diplopia			

subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Dry Eye			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Erythema of Eyelid			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Eye Discharge			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Eye Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Eye Inflammation			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Eye Irritation			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Eye Pain			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Eye Pruritus			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Eyelid Haematoma			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Eyelid Oedema			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Glaucoma			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	4	
Intraocular Haematoma			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Lacrimation Increased			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	1	5	
Meibomian Gland Dysfunction			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Miosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ocular Hyperaemia			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Orbital Oedema			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Periorbital Oedema			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Periorbital Pain			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Periorbital Swelling			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Photophobia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Retinal Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Retinal Tear			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Retinopathy Hypertensive			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rhegmatogenous Retinal Detachment			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Swelling of Eyelid			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Tolosa-Hunt Syndrome			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Vision Blurred			
subjects affected / exposed	2 / 354 (0.56%)	5 / 346 (1.45%)	
occurrences (all)	2	5	
Visual Acuity Reduced			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Visual Impairment			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Vitreous Detachment			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	5 / 354 (1.41%)	14 / 346 (4.05%)	
occurrences (all)	6	23	
Abdominal Distension			
subjects affected / exposed	8 / 354 (2.26%)	8 / 346 (2.31%)	
occurrences (all)	8	8	
Abdominal Hernia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Abdominal Pain			

subjects affected / exposed	25 / 354 (7.06%)	26 / 346 (7.51%)	
occurrences (all)	28	30	
Abdominal Pain Lower			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Abdominal Pain Upper			
subjects affected / exposed	13 / 354 (3.67%)	21 / 346 (6.07%)	
occurrences (all)	16	26	
Abdominal Tenderness			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Anal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Angular Cheilitis			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Aphthous Ulcer			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	4	
Breath Odour			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Cheilitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Chronic Gastritis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Colitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Constipation			

subjects affected / exposed	64 / 354 (18.08%)	64 / 346 (18.50%)	
occurrences (all)	76	85	
Dental Caries			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Dental Cyst			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	87 / 354 (24.58%)	100 / 346 (28.90%)	
occurrences (all)	143	168	
Diverticulum Intestinal			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Dry Mouth			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Duodenal Ulcer			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	3	
Duodenogastric Reflux			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	12 / 354 (3.39%)	22 / 346 (6.36%)	
occurrences (all)	12	25	
Dysphagia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Enteritis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Enterocolitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	4	
Epigastric Discomfort			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Flatulence			
subjects affected / exposed	3 / 354 (0.85%)	1 / 346 (0.29%)	
occurrences (all)	3	1	
Food Poisoning			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Gastric Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Gastric Polyps			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gastric Xanthoma			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	3 / 354 (0.85%)	4 / 346 (1.16%)	
occurrences (all)	4	5	
Gastritis Erosive			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Gastrointestinal Disorder			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gastrointestinal Toxicity			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 354 (0.56%)	5 / 346 (1.45%)	
occurrences (all)	2	5	
Gingival Bleeding			

subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Gingival Discomfort			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gingival Swelling			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	4 / 354 (1.13%)	6 / 346 (1.73%)	
occurrences (all)	4	6	
Hiatus Hernia			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Ileus Paralytic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Inguinal Hernia			
subjects affected / exposed	0 / 354 (0.00%)	6 / 346 (1.73%)	
occurrences (all)	0	6	
Intra-Abdominal Haematoma			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Irritable Bowel Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Large Intestine Polyp			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Loose Tooth			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Melaena			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Mouth Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Mouth Ulceration			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	76 / 354 (21.47%)	76 / 346 (21.97%)	
occurrences (all)	113	139	
Odynophagia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Oesophagitis			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Oral Cavity Fistula			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Oral Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Oral Pain			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	3	
Pancreatitis Acute			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Paraesthesia Oral			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Parotid Gland Enlargement			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Periodontal Disease			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rectal Haemorrhage			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Rectal Polyp			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	2	
Salivary Gland Mass			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Salivary Hypersecretion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	10 / 354 (2.82%)	10 / 346 (2.89%)	
occurrences (all)	12	10	
Tooth Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Tooth Loss			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 354 (0.00%)	6 / 346 (1.73%)	
occurrences (all)	0	6	
Ulcerative Gastritis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Umbilical Hernia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Vomiting			

subjects affected / exposed	52 / 354 (14.69%)	62 / 346 (17.92%)	
occurrences (all)	76	100	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Actinic Keratosis			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Alopecia			
subjects affected / exposed	3 / 354 (0.85%)	4 / 346 (1.16%)	
occurrences (all)	3	4	
Blister			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	4	1	
Decubitus Ulcer			
subjects affected / exposed	3 / 354 (0.85%)	4 / 346 (1.16%)	
occurrences (all)	3	5	
Dermal Cyst			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Dermatitis			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Dermatitis Allergic			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Dermatitis Atopic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Dermatitis Contact			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Dermatitis Exfoliative Generalised			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Drug Eruption			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Dry Skin			
subjects affected / exposed	3 / 354 (0.85%)	6 / 346 (1.73%)	
occurrences (all)	3	7	
Ecchymosis			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	3	2	
Eczema			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Eczema Asteatotic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Eczema Nummular			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	3 / 354 (0.85%)	9 / 346 (2.60%)	
occurrences (all)	8	10	
Erythema Multiforme			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Exfoliative Rash			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Guttate Psoriasis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Haemorrhage Subcutaneous			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 354 (0.28%)	6 / 346 (1.73%)	
occurrences (all)	1	6	

Hyperkeratosis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Hypertrophic Scar			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Lichenoid Keratosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Nail Discolouration			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Nail Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Night Sweats			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Papule			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Petechiae			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Pruritus			
subjects affected / exposed	11 / 354 (3.11%)	28 / 346 (8.09%)	
occurrences (all)	13	39	
Purpura Senile			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	49 / 354 (13.84%)	40 / 346 (11.56%)	
occurrences (all)	74	54	
Rash Erythematous			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	

Rash Macular			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Rash Maculo-Papular			
subjects affected / exposed	7 / 354 (1.98%)	2 / 346 (0.58%)	
occurrences (all)	8	2	
Rash Papular			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Rash Pruritic			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Skin Erosion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	3	
Skin Exfoliation			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Skin Haemorrhage			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Skin Hyperpigmentation			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Skin Induration			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Skin Lesion			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Skin Mass			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Skin Reaction			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	

Skin Ulcer			
subjects affected / exposed	4 / 354 (1.13%)	1 / 346 (0.29%)	
occurrences (all)	6	1	
Solar Dermatitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Solar Lentigo			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Toxic Skin Eruption			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	4	0	
Urticaria			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	4	
Urticaria Papular			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Xeroderma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	3 / 354 (0.85%)	6 / 346 (1.73%)	
occurrences (all)	4	7	
Albuminuria			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Anuria			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Azotaemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Calculus Bladder			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Calculus Urinary			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Chronic Kidney Disease			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	2	5	
Cystitis Haemorrhagic			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	3 / 354 (0.85%)	13 / 346 (3.76%)	
occurrences (all)	3	16	
Glycosuria			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	4	
Hypertonic Bladder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Incontinence			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Leukocyturia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Nephrolithiasis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Nocturia			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	2	2	
Pollakiuria			

subjects affected / exposed	5 / 354 (1.41%)	3 / 346 (0.87%)	
occurrences (all)	5	3	
Polyuria			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal Atrophy			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal Colic			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Renal Cyst			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal Failure			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences (all)	2	6	
Renal Impairment			
subjects affected / exposed	8 / 354 (2.26%)	8 / 346 (2.31%)	
occurrences (all)	9	12	
Renal Injury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Renal Pain			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Strangury			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Urethral Stenosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Urinary Incontinence			

subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	5	
Urinary Retention			
subjects affected / exposed	2 / 354 (0.56%)	2 / 346 (0.58%)	
occurrences (all)	3	2	
Urinary Tract Obstruction			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Urinary Tract Pain			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Adrenal Insufficiency			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Autoimmune Thyroiditis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Goitre			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Hyperthyroidism			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Inappropriate Antidiuretic Hormone Secretion			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Steroid Withdrawal Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Thyroid Disorder			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Thyroid Mass			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 354 (6.21%)	49 / 346 (14.16%)	
occurrences (all)	24	68	
Arthritis			
subjects affected / exposed	4 / 354 (1.13%)	4 / 346 (1.16%)	
occurrences (all)	5	5	
Back Pain			
subjects affected / exposed	40 / 354 (11.30%)	67 / 346 (19.36%)	
occurrences (all)	48	109	
Bone Pain			
subjects affected / exposed	8 / 354 (2.26%)	27 / 346 (7.80%)	
occurrences (all)	11	35	
Bursitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Coccydynia			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Exostosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Exposed Bone in Jaw			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Fistula			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Flank Pain			

subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Gouty Arthritis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Groin Pain			
subjects affected / exposed	3 / 354 (0.85%)	2 / 346 (0.58%)	
occurrences (all)	4	2	
Haematoma Muscle			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Intervertebral Disc Compression			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Intervertebral Disc Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Joint Effusion			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Joint Range of Motion Decreased			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Joint Swelling			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Limb Discomfort			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Muscle Contracture			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Muscle Fatigue			

subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Muscle Oedema			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Muscle Spasms			
subjects affected / exposed	9 / 354 (2.54%)	12 / 346 (3.47%)	
occurrences (all)	11	18	
Muscle Tightness			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Muscular Weakness			
subjects affected / exposed	8 / 354 (2.26%)	4 / 346 (1.16%)	
occurrences (all)	9	6	
Musculoskeletal Chest Pain			
subjects affected / exposed	11 / 354 (3.11%)	18 / 346 (5.20%)	
occurrences (all)	11	23	
Musculoskeletal Discomfort			
subjects affected / exposed	0 / 354 (0.00%)	5 / 346 (1.45%)	
occurrences (all)	0	5	
Musculoskeletal Pain			
subjects affected / exposed	10 / 354 (2.82%)	22 / 346 (6.36%)	
occurrences (all)	10	30	
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	5 / 354 (1.41%)	18 / 346 (5.20%)	
occurrences (all)	8	20	
Myofascial Pain Syndrome			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Myopathy			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Neck Pain			

subjects affected / exposed	1 / 354 (0.28%)	15 / 346 (4.34%)	
occurrences (all)	1	17	
Osteitis			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Osteoarthritis			
subjects affected / exposed	2 / 354 (0.56%)	6 / 346 (1.73%)	
occurrences (all)	2	6	
Osteochondrosis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Osteonecrosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Osteonecrosis of Jaw			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Osteopenia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Osteoporosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pain in Extremity			
subjects affected / exposed	22 / 354 (6.21%)	40 / 346 (11.56%)	
occurrences (all)	30	54	
Pain in Jaw			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pathological Fracture			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Periostitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	3	
Pubic Pain			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Rhabdomyolysis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Scleroderma			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Sjogren's Syndrome			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Spinal Osteoarthritis			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	6	
Spinal Pain			
subjects affected / exposed	1 / 354 (0.28%)	11 / 346 (3.18%)	
occurrences (all)	1	16	
Spinal Segmental Dysfunction			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Spinal Stenosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Synovial Cyst			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Temporomandibular Joint Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Tendon Disorder			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Tendonitis			

subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Tenosynovitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Trigger Finger			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Vertebral Foraminal Stenosis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess Jaw			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Alveolar Osteitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Appendicitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Arthritis Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Blister Infected			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Body Tinea			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Bronchitis			
subjects affected / exposed	25 / 354 (7.06%)	71 / 346 (20.52%)	
occurrences (all)	27	102	
Bronchitis Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Bronchopulmonary Aspergillosis				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Candida Infection				
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)		
occurrences (all)	0	4		
Cellulitis				
subjects affected / exposed	5 / 354 (1.41%)	5 / 346 (1.45%)		
occurrences (all)	8	5		
Cervicitis				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Clostridium Colitis				
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)		
occurrences (all)	2	0		
Conjunctivitis				
subjects affected / exposed	10 / 354 (2.82%)	12 / 346 (3.47%)		
occurrences (all)	15	13		
Covid-19				
subjects affected / exposed	0 / 354 (0.00%)	25 / 346 (7.23%)		
occurrences (all)	0	26		
Covid-19 Pneumonia				
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)		
occurrences (all)	0	2		
Cystitis				
subjects affected / exposed	2 / 354 (0.56%)	8 / 346 (2.31%)		
occurrences (all)	2	10		
Cytomegalovirus Infection				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Cytomegalovirus Infection Reactivation				
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)		
occurrences (all)	0	1		
Dermo-Hypodermitis				

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Device Related Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Diverticulitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Dysentery			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Ear Infection			
subjects affected / exposed	3 / 354 (0.85%)	3 / 346 (0.87%)	
occurrences (all)	3	4	
Encephalitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Enteritis Infectious			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Enterococcal Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Enterocolitis Infectious			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Enterocolitis Viral			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Epididymitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Escherichia Bacteraemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Escherichia Infection			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Eye Abscess			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Eye Infection			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Eye Infection Viral			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	3 / 354 (0.85%)	0 / 346 (0.00%)	
occurrences (all)	4	0	
Fungal Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Fungal Skin Infection			
subjects affected / exposed	3 / 354 (0.85%)	3 / 346 (0.87%)	
occurrences (all)	3	3	
Furuncle			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Gastritis Viral			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 354 (0.28%)	11 / 346 (3.18%)	
occurrences (all)	1	13	
Gastroenteritis Adenovirus			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis Viral			

subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Gastrointestinal Infection			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	1	5	
Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	4	
Hepatitis B			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hepatitis C			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Herpes Simplex			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	3	
Herpes Virus Infection			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Herpes Zoster			
subjects affected / exposed	12 / 354 (3.39%)	22 / 346 (6.36%)	
occurrences (all)	12	31	
Herpes Zoster Reactivation			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	6 / 354 (1.69%)	1 / 346 (0.29%)	
occurrences (all)	8	1	
Infection			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Infective Myositis			

subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	10 / 354 (2.82%)	23 / 346 (6.65%)	
occurrences (all)	10	25	
Laryngitis			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Laryngitis Bacterial			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Localised Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	4	
Lower Respiratory Tract Infection			
subjects affected / exposed	11 / 354 (3.11%)	9 / 346 (2.60%)	
occurrences (all)	13	15	
Lower Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Meningitis Pneumococcal			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Metapneumovirus Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Myringitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Nail Infection			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	3	
Nasal Herpes			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	

Nasopharyngitis			
subjects affected / exposed	22 / 354 (6.21%)	50 / 346 (14.45%)	
occurrences (all)	25	99	
Oesophageal Candidiasis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Onychomycosis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Oral Candidiasis			
subjects affected / exposed	8 / 354 (2.26%)	9 / 346 (2.60%)	
occurrences (all)	9	10	
Oral Herpes			
subjects affected / exposed	0 / 354 (0.00%)	8 / 346 (2.31%)	
occurrences (all)	0	8	
Oropharyngeal Candidiasis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Osteomyelitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Osteomyelitis Chronic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Otitis Externa			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	3	
Otitis Media			
subjects affected / exposed	0 / 354 (0.00%)	5 / 346 (1.45%)	
occurrences (all)	0	5	
Otitis Media Acute			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	

Paronychia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Perichondritis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Periodontitis			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	2	
Peritonitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Peritonsillar Abscess			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	9 / 354 (2.54%)	14 / 346 (4.05%)	
occurrences (all)	10	18	
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	7 / 354 (1.98%)	39 / 346 (11.27%)	
occurrences (all)	8	47	
Pneumonia Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Pneumonia Viral			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Prostate Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pseudomonas Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

Pulmonary Sepsis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pulpitis Dental			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	4	
Pyelonephritis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis Acute			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pyelonephritis Chronic			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Pyuria			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Respiratory Tract Infection			
subjects affected / exposed	1 / 354 (0.28%)	22 / 346 (6.36%)	
occurrences (all)	1	38	
Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Respiratory Tract Infection Viral			
subjects affected / exposed	3 / 354 (0.85%)	9 / 346 (2.60%)	
occurrences (all)	3	12	
Rhinitis			
subjects affected / exposed	0 / 354 (0.00%)	7 / 346 (2.02%)	
occurrences (all)	0	7	
Rotavirus Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Septic Shock			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Sinusitis			
subjects affected / exposed	1 / 354 (0.28%)	13 / 346 (3.76%)	
occurrences (all)	1	14	
Skin Bacterial Infection			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Skin Candida			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Skin Infection			
subjects affected / exposed	1 / 354 (0.28%)	3 / 346 (0.87%)	
occurrences (all)	1	3	
Streptococcal Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Streptococcal Sepsis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Subcutaneous Abscess			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Systemic Bacterial Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Tinea Infection			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	2	
Tonsillitis			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Tooth Abscess			
subjects affected / exposed	0 / 354 (0.00%)	3 / 346 (0.87%)	
occurrences (all)	0	4	
Tooth Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

Tracheitis			
subjects affected / exposed	3 / 354 (0.85%)	2 / 346 (0.58%)	
occurrences (all)	3	2	
Tracheobronchitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Tracheobronchitis Viral			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	2	0	
Tracheostomy Infection			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	48 / 354 (13.56%)	103 / 346 (29.77%)	
occurrences (all)	64	235	
Urinary Tract Infection			
subjects affected / exposed	13 / 354 (3.67%)	43 / 346 (12.43%)	
occurrences (all)	20	68	
Urinary Tract Infection Bacterial			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Urosepsis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Vaginal Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Varicella Zoster Virus Infection			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Viral Infection			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	6	
Viral Pharyngitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	

Viral Rhinitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 354 (0.28%)	5 / 346 (1.45%)	
occurrences (all)	2	5	
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Wound Infection			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	2 / 354 (0.56%)	1 / 346 (0.29%)	
occurrences (all)	2	1	
Decreased Appetite			
subjects affected / exposed	46 / 354 (12.99%)	42 / 346 (12.14%)	
occurrences (all)	66	60	
Dehydration			
subjects affected / exposed	11 / 354 (3.11%)	10 / 346 (2.89%)	
occurrences (all)	14	14	
Diabetes Mellitus			
subjects affected / exposed	5 / 354 (1.41%)	3 / 346 (0.87%)	
occurrences (all)	5	3	
Dyslipidaemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Fluid Overload			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Fluid Retention			

subjects affected / exposed	1 / 354 (0.28%)	6 / 346 (1.73%)	
occurrences (all)	1	6	
Folate Deficiency			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Glucose Tolerance Impaired			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	1 / 354 (0.28%)	2 / 346 (0.58%)	
occurrences (all)	1	2	
Hyperamylasaemia			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	3	
Hypercalcaemia			
subjects affected / exposed	5 / 354 (1.41%)	0 / 346 (0.00%)	
occurrences (all)	7	0	
Hypercholesterolaemia			
subjects affected / exposed	2 / 354 (0.56%)	3 / 346 (0.87%)	
occurrences (all)	2	3	
Hyperglycaemia			
subjects affected / exposed	13 / 354 (3.67%)	26 / 346 (7.51%)	
occurrences (all)	29	42	
Hyperkalaemia			
subjects affected / exposed	7 / 354 (1.98%)	16 / 346 (4.62%)	
occurrences (all)	7	33	
Hyperlipidaemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hypernatraemia			
subjects affected / exposed	3 / 354 (0.85%)	5 / 346 (1.45%)	
occurrences (all)	7	12	
Hyperphosphataemia			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			

subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	2	
Hyperuricaemia			
subjects affected / exposed	6 / 354 (1.69%)	14 / 346 (4.05%)	
occurrences (all)	8	24	
Hypoalbuminaemia			
subjects affected / exposed	5 / 354 (1.41%)	12 / 346 (3.47%)	
occurrences (all)	5	14	
Hypocalcaemia			
subjects affected / exposed	18 / 354 (5.08%)	23 / 346 (6.65%)	
occurrences (all)	28	33	
Hypoglycaemia			
subjects affected / exposed	4 / 354 (1.13%)	5 / 346 (1.45%)	
occurrences (all)	4	10	
Hypokalaemia			
subjects affected / exposed	17 / 354 (4.80%)	26 / 346 (7.51%)	
occurrences (all)	24	41	
Hypomagnesaemia			
subjects affected / exposed	3 / 354 (0.85%)	5 / 346 (1.45%)	
occurrences (all)	3	6	
Hyponatraemia			
subjects affected / exposed	10 / 354 (2.82%)	12 / 346 (3.47%)	
occurrences (all)	11	15	
Hypophagia			
subjects affected / exposed	2 / 354 (0.56%)	0 / 346 (0.00%)	
occurrences (all)	3	0	
Hypophosphataemia			
subjects affected / exposed	4 / 354 (1.13%)	1 / 346 (0.29%)	
occurrences (all)	6	1	
Hypoproteinaemia			
subjects affected / exposed	0 / 354 (0.00%)	2 / 346 (0.58%)	
occurrences (all)	0	3	
Impaired Fasting Glucose			
subjects affected / exposed	1 / 354 (0.28%)	0 / 346 (0.00%)	
occurrences (all)	1	0	
Iron Deficiency			

subjects affected / exposed	1 / 354 (0.28%)	6 / 346 (1.73%)	
occurrences (all)	1	7	
Malnutrition			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Marasmus			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Obesity			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Steroid Diabetes			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Tumour Lysis Syndrome			
subjects affected / exposed	1 / 354 (0.28%)	1 / 346 (0.29%)	
occurrences (all)	1	1	
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 354 (0.00%)	4 / 346 (1.16%)	
occurrences (all)	0	4	
Vitamin B12 Deficiency			
subjects affected / exposed	1 / 354 (0.28%)	4 / 346 (1.16%)	
occurrences (all)	1	4	
Vitamin D Deficiency			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	
Zinc Deficiency			
subjects affected / exposed	0 / 354 (0.00%)	1 / 346 (0.29%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2014	The overall reason for the amendment was to incorporate investigator feedback into the protocol, to further clarify MRD monitoring, to clarify safety reporting requirements for sites in Japan, to incorporate updated IMWG criteria
05 November 2015	The overall reason for the amendment was to provide updated guidance with respect to VELCADE dose modifications (per the Summary of Product Characteristics [SmPC] and United Sates Package Insert [USPI]) and to align with the VELCADE label regarding dose modifications, to incorporate investigator feedback into the protocol, and to revise operational aspects of the study and provide clarifications on study procedures.
25 July 2016	The overall reason for the amendment was the Safety Evaluations included in Protocol Amendment 2 (dated 05 Nov 2015) for the chemistry panel (that is, the analysis of sodium and potassium levels) would require the collection of results to be done retrospectively from the date of participant consent for the duration of the study, if collected as part of routine care. The baseline data, if available, were needed in order to effectively analyze safety with respect to changes in sodium/potassium levels while on treatment with respect to the investigational agent daratumumab in this combination with VMP in the frontline setting of treatment for multiple myeloma in an elderly population. This does not require any additional testing nor does it required a change to the Informed Consent Form or the request for additional consent from the participants.
11 November 2016	The overall reason for the amendment was the International Myeloma Working Group (IMWG) had recently defined new categories of Minimal Residual Disease (MRD)–negativity and had clarified several aspects of disease response assessment along with clinical trial endpoints (Kumar, 2016). In order for Protocol MMY3007 to be aligned with the new categories of MRD-negativity, the time points for collection of bone marrow for MRD assessment must be revised.
14 February 2018	The overall reason for the amendment was based on the Independent Data Monitoring Committee (IDMC) recommendation following review of data from the second interim analysis, the study was amended to allow participants in Arm A (VELCADE [bortezomib]-melphalan-prednisone [VMP] alone) access to daratumumab after sponsor confirmation of disease progression (PD) per International Myeloma Working Group criteria.
26 June 2019	The overall reason for the amendment was in response to identification of a new important risk (hepatitis B virus [HBV] reactivation).
16 December 2019	The overall reason for the amendment was to allow participants in Treatment Arm B receiving daratumumab IV (16 mg/kg) the option to switch to daratumumab subcutaneous (1800 mg), at the discretion of the investigator.
02 June 2021	The overall reason for this amendment was to define the final overall survival (OS) analysis cutoff and the corresponding end of the electronic case report form (eCRF) data collection. Additionally, this amendment allows participants who were benefiting from treatment with daratumumab had the option to continue to receive study treatment after the final OS analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported