



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
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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 $9 \text{ mg}/\text{m}^2$ orally once daily (QD) on Days 1 to 4 and prednisone $60 \text{ mg}/\text{m}^2$ 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 $1.3 \text{ mg}/\text{m}^2$ 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 $60 \text{ mg}/\text{m}^2$ 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 $9 \text{ mg}/\text{m}^2$ orally QD on Days 1 to 4 of each cycle up to Cycle 9.

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

Participants received Velcade 1.3 mg/m² 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/m², orally QD on Days 1-4 and prednisone 60 mg/m², 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/m² 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/m² 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/m² 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)
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Reporting group description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m²) 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/m² orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m² 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)
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Reporting group description:

Participants received Velcade 1.3 mg/m² 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/m², orally QD on Days 1-4 and prednisone 60 mg/m², 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 (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
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 >10 mg/dL); Only participants without measurable serum and urine M-protein levels, without measurable disease by FLC levels, bone marrow Plasma cells(PC)% (absolute% $\geq 10\%$);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 >11.5 mg/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 (\geq) 50 percentage (%) reduction of serum M-protein and reduction in 24 hour urinary M-protein by \geq 90% or to less than ($<$) 200 mg/24 hours, if serum and urine M-protein are not measurable, decrease of \geq 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, \geq 50% reduction in bone marrow plasma cells (PC) was required in place of M-protein, provided baseline bone marrow PC percentage was \geq 30%, in addition to above criteria, if present at baseline, a \geq 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
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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 $\geq 90\%$ 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
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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 Complete Response (CR) or Better

End point title	Percentage of Participants With Complete Response (CR) or Better
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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
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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 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 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: Progression Free Survival on Next Line of Therapy (PFS2)

End point title	Progression Free Survival on Next Line of Therapy (PFS2)
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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
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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: Time to Disease Progression (TTP)

End point title	Time to Disease Progression (TTP)
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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 $\geq 0.5\text{g/dL}$); Urine M-component (absolute increase $\geq 200\text{mg/24hours}$); Only in participants without measurable serum and urine M-protein levels: difference between involved and uninvolved FLC levels (absolute increase $>10\text{mg/dL}$); Only in participants without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow PC% (absolute% $\geq 10\%$); 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 $>11.5\text{mg/dL}$) 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
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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: $\geq 50\%$ reduction of serum and reduction in 24hour(h) urinary M-protein by $\geq 90\%$ or to $< 200\text{mg}/24\text{h}$; If serum and urine M-protein were not measurable, decrease of $\geq 50\%$ 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, $\geq 50\%$ reduction in bone marrow PCs required in place of M-protein, provided baseline bone marrow PC% $\geq 30\%$; if present at baseline, $\geq 50\%$ 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: 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 \geq 0.5g/dL);Urine M-component(absolute increase \geq 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% \geq 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
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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
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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
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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
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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)
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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 Analogue 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
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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 (\pm 23.856)	13.94 (\pm 21.984)		
Month 42; n=33, 123	12.88 (\pm 23.789)	14.33 (\pm 21.502)		
Month 48; n=23, 99	9.17 (\pm 18.612)	11.93 (\pm 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
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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
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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 (\pm 0.312)	0.12 (\pm 0.266)		
Month 6; n= 210, 230	0.12 (\pm 0.269)	0.14 (\pm 0.271)		
Month 9; n= 185, 227	0.16 (\pm 0.27)	0.16 (\pm 0.271)		
Month 12; n= 185, 217	0.15 (\pm 0.281)	0.17 (\pm 0.288)		
Month 18; n= 134, 194	0.14 (\pm 0.268)	0.17 (\pm 0.293)		
Month 24; n= 82, 150	0.15 (\pm 0.252)	0.18 (\pm 0.312)		
Month 30; n= 71, 157	0.16 (\pm 0.291)	0.19 (\pm 0.303)		
Month 36; n= 47, 143	0.16 (\pm 0.315)	0.21 (\pm 0.306)		
Month 42; n= 33, 123	0.08 (\pm 0.303)	0.2 (\pm 0.287)		
Month 48; n= 23, 99	0.07 (\pm 0.246)	0.15 (\pm 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
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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 % $\geq 10\%$); 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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Velcade, Melphalan and Prednisone (VMP)
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Reporting group description:

Participants received Velcade (bortezomib) 1.3 milligrams per square meter (mg/m²) 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/m² orally once daily (QD) on Days 1 to 4 and prednisone 60 mg/m² 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)
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Reporting group description:

Participants received Velcade 1.3 mg/m² 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/m², orally QD on Days 1-4 and prednisone 60 mg/m², 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 occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Venous Thrombosis Limb subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Surgical and medical procedures Transurethral Prostatectomy subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	43 / 354 (12.15%) 72	51 / 346 (14.74%) 95	
Catheter Site Pain subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Catheter Site Phlebitis subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Chest Discomfort subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	4 / 346 (1.16%) 4	
Chest Pain subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	4 / 346 (1.16%) 4	
Chills subjects affected / exposed occurrences (all)	6 / 354 (1.69%) 8	28 / 346 (8.09%) 32	
Crepitations subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Discomfort subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	1 / 346 (0.29%) 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 occurrences (all)	3 / 354 (0.85%) 3	3 / 346 (0.87%) 3	
Mood Swings subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Nervousness subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	4 / 346 (1.16%) 5	
Psychiatric Decompensation subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	2 / 346 (0.58%) 2	
Restlessness subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	2 / 346 (0.58%) 2	
Sleep Disorder subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 2	0 / 346 (0.00%) 0	
Somatic Symptom Disorder subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Substance-Induced Psychotic Disorder subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 346 (0.29%) 1	
Tension subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Product issues Device Occlusion subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Hepatobiliary disorders Cholecystitis subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 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 occurrences (all)	1 / 354 (0.28%) 1	6 / 346 (1.73%) 11	
Injury, poisoning and procedural complications			
Anaemia Postoperative subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Ankle Fracture subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Arthropod Bite subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Bone Contusion subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Clavicle Fracture subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Compression Fracture subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Concussion subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Contusion subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	15 / 346 (4.34%) 17	
Craniocerebral Injury subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Ear Injury subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 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 occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Traumatic Haemorrhage subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Upper Limb Fracture subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 346 (0.58%) 2	
Wound subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 346 (0.29%) 1	
Wound Dehiscence subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Wound Haemorrhage subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Wrist Fracture subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 346 (0.29%) 1	
Congenital, familial and genetic disorders			
Hydrocele subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 346 (0.00%) 0	
Hypertrophic Cardiomyopathy subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Cardiac disorders			
Angina Pectoris subjects affected / exposed occurrences (all)	4 / 354 (1.13%) 4	6 / 346 (1.73%) 8	
Aortic Valve Disease subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 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
Drizzling		
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 occurrences (all)	52 / 354 (14.69%) 76	62 / 346 (17.92%) 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 occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Thyroid Mass subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	22 / 354 (6.21%) 24	49 / 346 (14.16%) 68	
Arthritis subjects affected / exposed occurrences (all)	4 / 354 (1.13%) 5	4 / 346 (1.16%) 5	
Back Pain subjects affected / exposed occurrences (all)	40 / 354 (11.30%) 48	67 / 346 (19.36%) 109	
Bone Pain subjects affected / exposed occurrences (all)	8 / 354 (2.26%) 11	27 / 346 (7.80%) 35	
Bursitis subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Coccydynia subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 346 (0.29%) 1	
Exostosis subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Exposed Bone in Jaw subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1	
Fistula subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 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 occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1
Candida Infection subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	4 / 346 (1.16%) 4
Cellulitis subjects affected / exposed occurrences (all)	5 / 354 (1.41%) 8	5 / 346 (1.45%) 5
Cervicitis subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1
Clostridium Colitis subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	0 / 346 (0.00%) 0
Conjunctivitis subjects affected / exposed occurrences (all)	10 / 354 (2.82%) 15	12 / 346 (3.47%) 13
Covid-19 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	25 / 346 (7.23%) 26
Covid-19 Pneumonia subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 346 (0.58%) 2
Cystitis subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	8 / 346 (2.31%) 10
Cytomegalovirus Infection subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1
Cytomegalovirus Infection Reactivation subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 346 (0.29%) 1
Dermo-Hypodermatitis		

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 States 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