Clinical trial results:
A Phase III Study of Lenalidomide and Low-Dose Dexamethasone With or Without Pembrolizumab (MK3475) in Newly Diagnosed and Treatment Naïve Multiple Myeloma (KEYNOTE 185).

Summary

EudraCT number	2015-002901-12
Trial protocol	DE ES IE FR IT
Global end of trial date	07 July 2020

Results information

Result version number	v1 (current)
This version publication date	15 July 2021
First version publication date	15 July 2021

Trial information

Trial identification

Sponsor protocol code	MK-3475-185

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02579863
WHO universal trial number (UTN)	-
Other trial identifiers	US National Clinical Trial (NCT) unique identifier: NCT02579863, Study Name: KEYNOTE 185

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	07 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 July 2018
Global end of trial reached?	Yes
Global end of trial date	07 July 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to compare the progression-free survival (PFS) as assessed by Clinical Adjudication Committee (CAC) blinded central review according to the International Myeloma Working Group response criteria (IMWG criteria) between treatment arms.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 22
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 52
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Norway: 17
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 95
Worldwide total number of subjects	310
EEA total number of subjects	71

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)	6
From 65 to 84 years	288
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 140 centers in 15 countries.
The database cutoff date was August 3, 2020.

Note: Due to administrative reasons (a noncompliant site), 2 participants in the Pembrolizumab plus SOC arm and one participant in the SOC arm, were recorded as "Ongoing in Trial" in the CSR Disposition Table and "Final Disposition Unknown" here.

Pre-assignment

Screening details:

1. Had a confirmed diagnosis of active multiple myeloma and measurable disease as defined in the protocol.
2. Was ineligible to receive treatment with autologous stem cell transplant (auto-SCT) due to age (≥65 years old) or any significant coexisting medical condition. Subjects <65 years old who refused auto-SCT were not eligible for this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab + Lenalidomide + Dexamethasone

Arm description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle

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

Dosage and administration details:

Lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle

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

Dosage and administration details:

Dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles

Arm title	Standard of Care (SOC) Lenolidomide + Dexamethasone

Arm description:

Participants received lenalidomide 25 mg PO on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Arm type	Active comparator
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle

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

Dosage and administration details:

Dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles

Number of subjects in period 1	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone
Started	156	154
Treated	154	148
Completed	0	0
Not completed	156	154
Adverse event, serious fatal	31	29
Physician decision	1	2
Consent withdrawn by subject	20	20
Screen Failure	-	2
Adverse event, non-fatal	18	11
Final Disposition Unknown	2	1
Lost to follow-up	2	1
Study Terminated at Selected Sites	82	88

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab + Lenalidomide + Dexamethasone
Reporting group description:	
Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.	
Reporting group title	Standard of Care (SOC) Lenolidomide + Dexamethasone
Reporting group description:	
Participants received lenalidomide 25 mg PO on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.	

Reporting group values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone	Total
Number of subjects	156	154	310
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	1	6
From 65-84 years	144	144	288
85 years and over	7	9	16
Age Continuous Units: Years			
arithmetic mean	74.4	74.3	
standard deviation	± 6.0	± 5.9	-
Sex: Female, Male Units: Participants			
Female	85	81	166
Male	71	73	144
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	27	27	54
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	9	3	12
White	115	121	236
More than one race	1	0	1
Unknown or Not Reported	3	3	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	4	8
Not Hispanic or Latino	143	136	279

Unknown or Not Reported	9	14	23
International Stage (I, II, III).			
The International Staging System (ISS) defines the factors that influence patient survival. The system has 3 stages based on the measurement of serum albumin and the levels of serum β2-microglobulin (β2-M). Stage I: β2-M <3.5 mg/L with a serum albumin of 3.5 g/dL or more; Stage II: Either of these 2 criteria: β2-M between 3.5 mg/L and 5.5 mg/dL Albumin <3.5 g/dL; Stage III: β2-M >5.5 mg/L.			
Units: Subjects			
Stage I	39	53	92
Stage II	70	66	136
Stage III	46	34	80
Missing	1	1	2

End points

End points reporting groups

Reporting group title	Pembrolizumab + Lenalidomide + Dexamethasone

Reporting group description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Reporting group title	Standard of Care (SOC) Lenolidomide + Dexamethasone

Reporting group description:

Participants received lenalidomide 25 mg PO on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Primary: Progression Free Survival (PFS) Evaluated According to the International Myeloma Working Group (IMWG) Response Criteria 2011 by Clinical Adjudication Committee (CAC) Blinded Central Review

End point title	Progression Free Survival (PFS) Evaluated According to the International Myeloma Working Group (IMWG) Response Criteria 2011 by Clinical Adjudication Committee (CAC) Blinded Central Review

End point description:

PFS was defined as the time from randomization to the first documented disease progression (events of new bone lesions, soft tissue plasmacytomas or an increase in existing lesions, or death due to any cause). The median PFS was calculated from the product-limit (Kaplan-Meier) method for censored data. A relatively small number of events resulted in high variabilities and the inability to estimate certain parameters (i.e. medians and confidence limits). A value of "9999" indicates that at the time of data cut-off parameters could not be estimated. The analysis population included all randomized participants. Participants were included in the treatment group to which they were randomized. The data cutoff date was July 9, 2018.

End point type	Primary

End point timeframe:

Up to approximately 30 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	154		
Units: Months				
median (confidence interval 95%)	19.6 (15.3 to 9999)	9999 (15.5 to 9999)		

Statistical analyses

Statistical analysis title	MK-3475 200mg Q3W + SOC vs. Standard of Care

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by "Age" (<75 years vs >= 75

years) and “ISS stage” (I or II vs. III).

Comparison groups	Pembrolizumab + Lenalidomide + Dexamethasone v Standard of Care (SOC) Lenolidomide + Dexamethasone
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33475 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.45

Notes:

[1] - One-sided p-value based on Stratified log-rank test.

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from randomization to death due to any cause. OS was calculated from the product-limit (Kaplan-Meier) method for censored data. Participants without documented death at the time of the final analysis were censored at the date of the last follow-up. This is an event-driven (events of death) outcome measure. "9999" indicates that at the time of data cut-off, there were an insufficient number of events from the censored data to be able to estimate certain parameters (e.g. medians). The analysis population included all randomized participants. Participants were included in the treatment group to which they were randomized. The data cutoff date was August 3, 2020.

End point type	Secondary

End point timeframe:

Up to approximately 55 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	154		
Units: Months				
median (confidence interval 95%)	9999 (44.6 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	MK-3475 200mg Q3W + SOC vs. Standard of Care

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by “Age” (<75 years vs >= 75 years) and “ISS stage” (I or II vs. III).

Comparison groups	Pembrolizumab + Lenalidomide + Dexamethasone v Standard

	of Care (SOC) Lenolidomide + Dexamethasone
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.83416
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.84

Secondary: Overall Response Rate (ORR) Evaluated According to the IMWG Response Criteria by CAC Blinded Central Review

End point title	Overall Response Rate (ORR) Evaluated According to the IMWG Response Criteria by CAC Blinded Central Review

End point description:

ORR was based on participants who achieved at least a partial response (stringent complete response [sCR]+complete response [CR]+very good partial response [VGPR]+partial response [PR]) according to the IMWG. CR = negative immunofixation of serum and urine AND disappearance of any soft tissue plasmacytomas AND <5% plasmacytomas in the bone marrow; sCR=stringent complete response, CR as above PLUS normal serum free light-chain (FLC) assay ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence; VGPR = serum and urine M-component detectable by immunofixation but not on electrophoresis OR ≥ 90% reduction in serum M-component plus urine M-component <100 mg/24 hr; PR = ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg/24 hours. The analysis population included all randomized participants who were included in the treatment group to which they were randomized. The data cutoff date was July 9, 2018.

End point type	Secondary

End point timeframe:

Up to approximately 30 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	154		
Units: Percentage of participants				
number (confidence interval 95%)	74.4 (66.8 to 81.0)	68.8 (60.9 to 76.0)		

Statistical analyses

Statistical analysis title	MK-3475 200mg Q3W + SOC vs. Standard of Care

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by 'Age' (<75 years vs >= 75 years) and 'ISS stage' (I or II vs. III); If there were no participants in one of the treatment groups involved in a comparison for a particular stratum, then that stratum was excluded from the treatment comparison.

Comparison groups	Pembrolizumab + Lenalidomide + Dexamethasone v Standard of Care (SOC) Lenolidomide + Dexamethasone
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.13102
Method	One-sided p-value for testing
Parameter estimate	Difference in % vs SOC
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	15.8

Secondary: Duration of Response (DOR) Evaluated According to IMWG Response Criteria by CAC Blinded Central Review

End point title	Duration of Response (DOR) Evaluated According to IMWG Response Criteria by CAC Blinded Central Review

End point description:

Response duration was defined as the time from first documented evidence of at least a partial response (sCR+CR+VGPR+PR]), until confirmed disease progression or death. DOR was calculated from product-limit (Kaplan-Meier) method for censored data. This is an event-driven (events of disease progression and death) outcome measure. "9999" indicates that at the time of data cut-off, there were an insufficient number of events from the censored data to be able to estimate certain parameters (e.g. medians). Full Range is the minimum and maximum of the observed duration of response. The analysis population included all randomized participants who demonstrated at least a partial response. Participants were included in the treatment group to which they were randomized. The data cutoff date was July 9, 2018.

End point type	Secondary

End point timeframe:

Up to approximately 30 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	106		
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) Evaluated According to the IMWG Response Criteria by CAC blinded central review

End point title	Disease Control Rate (DCR) Evaluated According to the IMWG Response Criteria by CAC blinded central review

End point description:

Disease control rate was based on participants who achieved confirmed sCR, CR, VGPR, PR, or have demonstrated SD for at least 12 weeks prior to any evidence of progression. CR = negative immunofixation of serum and urine AND disappearance of any soft tissue plasmacytomas AND <5% plasmacytomas in the bone marrow; VGPR = serum and urine M-component detectable by immunofixation but not on electrophoresis OR ≥ 90% reduction in serum M-component plus urine M-component <100 mg/24 hr; PR = ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg/24 hours; SD = not meeting the criteria for CR, VGPR, PR, or PD; PD = development of new bone lesions or soft tissue plasmacytomas or on a definite increase in the size of existing bone lesions or soft tissue plasmacytomas. The analysis population included all randomized participants who included in the treatment group to which they were randomized. Data cutoff date was July 9, 2018.

End point type	Secondary

End point timeframe:

Up to approximately 30 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	154		
Units: Percentage of participants				
number (confidence interval 95%)	89.1 (83.1 to 93.5)	91.6 (86.0 to 95.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Second Progression Free Survival (PFS2)

End point title	Second Progression Free Survival (PFS2)

End point description:

PFS2 was defined as the time from randomization to subsequent disease progression after initiation of new anti-cancer therapy, or death from any cause, whichever occurred first, by investigator assessment. PFS was assessed by Clinical Adjudication Committee (CAC) blinded central review according to the

IMWG response criteria based on the development of new bone lesions or soft tissue plasmacytomas or on a definite increase in the size of existing bone lesions or soft tissue plasmacytomas. The analysis population included all randomized participants. Participants were included in the treatment group to which they were randomized. PFS2 was not completed due to incomplete enrollment for a clinical hold and study cancellation.

End point type	Secondary

End point timeframe:

Up to approximately 30 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - PFS2 was not completed due to incomplete enrollment for a clinical hold and study cancellation.

[3] - PFS2 was not completed due to incomplete enrollment for a clinical hold and study cancellation.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced One or More Adverse Events (AEs)

End point title	Number of Participants Who Experienced One or More Adverse Events (AEs)

End point description:

An AE was defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it was considered related to the medical treatment or procedure, that occurred during the course of the study. The analysis population consisted of all randomized participants who received at least one dose of study treatment. The database cutoff date was August 3, 2020.

End point type	Secondary

End point timeframe:

Up to approximately 55 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	148		
Units: Participants	152	141		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Discontinuing Study Treatment Due to an AE

End point title	Number of Participants Discontinuing Study Treatment Due to an AE

End point description:

An AE was defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it was considered related to the medical treatment or procedure, that occurred during the course of the study. The analysis population consisted of all randomized participants who received at least one dose of study treatment. The database cutoff date was August 3, 2020.

End point type	Secondary

End point timeframe:

Up to approximately 55 months

End point values	Pembrolizumab + Lenalidomide + Dexamethasone	Standard of Care (SOC) Lenolidomide + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	148		
Units: Participants	44	26		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 55 months

Adverse event reporting additional description:

The All-Cause Mortality analysis used all randomized participants whereas adverse events were collected for all treated participants. Disease progression of cancer under study was not considered an adverse event (AE) unless related to study treatment. The Database Cutoff Date was Aug. 3, 2020.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Pembrolizumab + Lenalidomide + Dexamethasone

Reporting group description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS lenalidomide 25 mg orally (PO) on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Reporting group title	Lenolidomide + Dexamethasone

Reporting group description:

Participants received lenalidomide 25 mg PO on Days 1 to 21 of each 21-day treatment cycle, and dexamethasone 40 mg PO on Days 1, 8, 15 and 22 of each 28-day cycle for up to 18 cycles.

Serious adverse events	Pembrolizumab + Lenalidomide + Dexamethasone	Lenolidomide + Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 154 (59.09%)	65 / 148 (43.92%)	
number of deaths (all causes)	51	43	
number of deaths resulting from adverse events	7	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (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			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 154 (0.65%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 154 (0.65%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypothermia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	8 / 154 (5.19%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	2 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 154 (0.65%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 154 (1.30%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 154 (1.95%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			

subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
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 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	8 / 154 (5.19%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	4 / 8	0 / 0	
deaths causally related to treatment / all	1 / 3	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 154 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	3 / 154 (1.95%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (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			
Accidental overdose			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 154 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	1 / 154 (0.65%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 154 (0.00%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial rupture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Fanconi syndrome			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (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	4 / 154 (2.60%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 154 (1.30%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiopulmonary failure			

subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 154 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Myocarditis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	3 / 154 (1.95%)	5 / 148 (3.38%)	
occurrences causally related to treatment / all	0 / 3	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytopenia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 154 (1.95%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	2 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	5 / 154 (3.25%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	5 / 154 (3.25%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic enteritis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nausea			

subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Vomiting			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (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			
Dermatitis exfoliative generalised			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			

subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 154 (3.90%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			

subjects affected / exposed	4 / 154 (2.60%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 154 (0.65%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 154 (1.95%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain in extremity			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torticollis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	2 / 154 (1.30%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 154 (1.95%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
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 / 154 (1.95%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	16 / 154 (10.39%)	10 / 148 (6.76%)	
occurrences causally related to treatment / all	9 / 19	1 / 10	
deaths causally related to treatment / all	1 / 3	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	8 / 154 (5.19%)	4 / 148 (2.70%)	
occurrences causally related to treatment / all	3 / 8	0 / 4	
deaths causally related to treatment / all	1 / 2	0 / 1	
Septic shock			
subjects affected / exposed	2 / 154 (1.30%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 154 (1.30%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 154 (1.30%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fulminant type 1 diabetes mellitus			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			

subjects affected / exposed	0 / 154 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 154 (0.65%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	2 / 154 (1.30%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 154 (0.65%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pembrolizumab + Lenalidomide + Dexamethasone	Lenolidomide + Dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	143 / 154 (92.86%)	129 / 148 (87.16%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	12 / 154 (7.79%)	8 / 148 (5.41%)	
occurrences (all)	13	9	

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 154 (7.14%)	17 / 148 (11.49%)	
occurrences (all)	11	20	
Fatigue			
subjects affected / exposed	44 / 154 (28.57%)	37 / 148 (25.00%)	
occurrences (all)	52	39	
Oedema			
subjects affected / exposed	8 / 154 (5.19%)	6 / 148 (4.05%)	
occurrences (all)	8	7	
Oedema peripheral			
subjects affected / exposed	25 / 154 (16.23%)	27 / 148 (18.24%)	
occurrences (all)	31	28	
Pyrexia			
subjects affected / exposed	29 / 154 (18.83%)	10 / 148 (6.76%)	
occurrences (all)	41	11	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 154 (12.99%)	18 / 148 (12.16%)	
occurrences (all)	21	19	
Dysphonia			
subjects affected / exposed	3 / 154 (1.95%)	10 / 148 (6.76%)	
occurrences (all)	6	10	
Dyspnoea			
subjects affected / exposed	19 / 154 (12.34%)	12 / 148 (8.11%)	
occurrences (all)	21	12	
Epistaxis			
subjects affected / exposed	8 / 154 (5.19%)	6 / 148 (4.05%)	
occurrences (all)	8	6	
Oropharyngeal pain			
subjects affected / exposed	8 / 154 (5.19%)	5 / 148 (3.38%)	
occurrences (all)	10	5	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	12 / 154 (7.79%)	11 / 148 (7.43%)	
occurrences (all)	14	12	

Depression			
subjects affected / exposed	9 / 154 (5.84%)	8 / 148 (5.41%)	
occurrences (all)	10	8	
Insomnia			
subjects affected / exposed	22 / 154 (14.29%)	27 / 148 (18.24%)	
occurrences (all)	25	33	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 154 (7.14%)	3 / 148 (2.03%)	
occurrences (all)	11	3	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 154 (5.19%)	1 / 148 (0.68%)	
occurrences (all)	8	1	
Neutrophil count decreased			
subjects affected / exposed	13 / 154 (8.44%)	12 / 148 (8.11%)	
occurrences (all)	23	23	
Weight decreased			
subjects affected / exposed	10 / 154 (6.49%)	17 / 148 (11.49%)	
occurrences (all)	10	18	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 154 (1.30%)	8 / 148 (5.41%)	
occurrences (all)	3	10	
Fall			
subjects affected / exposed	7 / 154 (4.55%)	9 / 148 (6.08%)	
occurrences (all)	10	12	
Nervous system disorders			
Dizziness			
subjects affected / exposed	14 / 154 (9.09%)	14 / 148 (9.46%)	
occurrences (all)	15	15	
Dysgeusia			
subjects affected / exposed	8 / 154 (5.19%)	12 / 148 (8.11%)	
occurrences (all)	8	12	
Headache			
subjects affected / exposed	9 / 154 (5.84%)	11 / 148 (7.43%)	
occurrences (all)	9	14	

Neuropathy peripheral			
subjects affected / exposed	9 / 154 (5.84%)	12 / 148 (8.11%)	
occurrences (all)	11	13	
Tremor			
subjects affected / exposed	11 / 154 (7.14%)	16 / 148 (10.81%)	
occurrences (all)	11	16	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	32 / 154 (20.78%)	27 / 148 (18.24%)	
occurrences (all)	48	40	
Neutropenia			
subjects affected / exposed	30 / 154 (19.48%)	26 / 148 (17.57%)	
occurrences (all)	54	51	
Thrombocytopenia			
subjects affected / exposed	12 / 154 (7.79%)	12 / 148 (8.11%)	
occurrences (all)	16	19	
Eye disorders			
Vision blurred			
subjects affected / exposed	11 / 154 (7.14%)	3 / 148 (2.03%)	
occurrences (all)	12	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	13 / 154 (8.44%)	13 / 148 (8.78%)	
occurrences (all)	16	18	
Constipation			
subjects affected / exposed	55 / 154 (35.71%)	33 / 148 (22.30%)	
occurrences (all)	62	35	
Diarrhoea			
subjects affected / exposed	36 / 154 (23.38%)	34 / 148 (22.97%)	
occurrences (all)	51	48	
Dry mouth			
subjects affected / exposed	12 / 154 (7.79%)	5 / 148 (3.38%)	
occurrences (all)	13	5	
Dyspepsia			
subjects affected / exposed	8 / 154 (5.19%)	2 / 148 (1.35%)	
occurrences (all)	9	2	
Nausea			

subjects affected / exposed	37 / 154 (24.03%)	33 / 148 (22.30%)	
occurrences (all)	54	38	
Stomatitis			
subjects affected / exposed	9 / 154 (5.84%)	6 / 148 (4.05%)	
occurrences (all)	11	6	
Vomiting			
subjects affected / exposed	30 / 154 (19.48%)	9 / 148 (6.08%)	
occurrences (all)	39	16	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	9 / 154 (5.84%)	3 / 148 (2.03%)	
occurrences (all)	9	3	
Night sweats			
subjects affected / exposed	8 / 154 (5.19%)	5 / 148 (3.38%)	
occurrences (all)	10	5	
Pruritus			
subjects affected / exposed	13 / 154 (8.44%)	5 / 148 (3.38%)	
occurrences (all)	17	5	
Rash			
subjects affected / exposed	32 / 154 (20.78%)	19 / 148 (12.84%)	
occurrences (all)	45	20	
Rash maculo-papular			
subjects affected / exposed	14 / 154 (9.09%)	11 / 148 (7.43%)	
occurrences (all)	19	13	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	13 / 154 (8.44%)	1 / 148 (0.68%)	
occurrences (all)	13	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 154 (11.04%)	9 / 148 (6.08%)	
occurrences (all)	21	12	
Back pain			
subjects affected / exposed	20 / 154 (12.99%)	17 / 148 (11.49%)	
occurrences (all)	24	21	
Muscle spasms			

subjects affected / exposed	14 / 154 (9.09%)	14 / 148 (9.46%)	
occurrences (all)	17	16	
Muscular weakness			
subjects affected / exposed	11 / 154 (7.14%)	4 / 148 (2.70%)	
occurrences (all)	12	5	
Musculoskeletal chest pain			
subjects affected / exposed	11 / 154 (7.14%)	7 / 148 (4.73%)	
occurrences (all)	11	7	
Musculoskeletal pain			
subjects affected / exposed	11 / 154 (7.14%)	10 / 148 (6.76%)	
occurrences (all)	14	11	
Pain in extremity			
subjects affected / exposed	9 / 154 (5.84%)	8 / 148 (5.41%)	
occurrences (all)	11	10	
Infections and infestations			
Bronchitis			
subjects affected / exposed	9 / 154 (5.84%)	4 / 148 (2.70%)	
occurrences (all)	12	5	
Nasopharyngitis			
subjects affected / exposed	11 / 154 (7.14%)	11 / 148 (7.43%)	
occurrences (all)	16	13	
Oral candidiasis			
subjects affected / exposed	15 / 154 (9.74%)	2 / 148 (1.35%)	
occurrences (all)	16	2	
Pneumonia			
subjects affected / exposed	11 / 154 (7.14%)	2 / 148 (1.35%)	
occurrences (all)	11	2	
Upper respiratory tract infection			
subjects affected / exposed	16 / 154 (10.39%)	13 / 148 (8.78%)	
occurrences (all)	16	17	
Urinary tract infection			
subjects affected / exposed	15 / 154 (9.74%)	12 / 148 (8.11%)	
occurrences (all)	16	16	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	26 / 154 (16.88%)	19 / 148 (12.84%)	
occurrences (all)	28	21	
Dehydration			
subjects affected / exposed	8 / 154 (5.19%)	5 / 148 (3.38%)	
occurrences (all)	14	6	
Gout			
subjects affected / exposed	8 / 154 (5.19%)	4 / 148 (2.70%)	
occurrences (all)	14	5	
Hyperglycaemia			
subjects affected / exposed	10 / 154 (6.49%)	8 / 148 (5.41%)	
occurrences (all)	17	12	
Hypocalcaemia			
subjects affected / exposed	16 / 154 (10.39%)	8 / 148 (5.41%)	
occurrences (all)	18	9	
Hypokalaemia			
subjects affected / exposed	26 / 154 (16.88%)	17 / 148 (11.49%)	
occurrences (all)	31	21	
Hypomagnesaemia			
subjects affected / exposed	10 / 154 (6.49%)	5 / 148 (3.38%)	
occurrences (all)	10	6	
Hyponatraemia			
subjects affected / exposed	9 / 154 (5.84%)	1 / 148 (0.68%)	
occurrences (all)	10	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 April 2016	a. Addition of Lenalidomide Adult Pregnancy Risk Minimization Plan for Clinical Trials. b. Removed, Embryo-Fetal Toxicity Associated with Lenalidomide. This information is now included in another section.
29 July 2016	Clarified the exclusion criteria related to pneumonitis
29 July 2016	a. Added treatment discontinuation statement with defined population. b. Added treatment discontinuation statement.
01 February 2017	a. Updated to permanently discontinue for any recurrent Grade 2 pneumonitis. b. Follow-up Visits; To collect additional information regarding allogeneic stem cell transplants and complications following treatment with pembrolizumab.
19 April 2018	a. Added in the second paragraph: Samples obtained for PK may be used to conduct additional safety analysis, if needed. b. Pharmacokinetic/anti-drug antibody (PK/ADA) samples may be used to conduct additional safety analysis, if needed. c. Samples obtained for PK or ADA may be used to conduct additional safety analysis, if needed.
09 July 2018	a. Updated duration of survival follow-up to 12 months following discontinuation visit. b. Updated follow-up after stem cell transplant (SCT) to provide for completion of follow-up at the end of the trial. c. Updated criteria for end of the trial to include Sponsor decision to close. d. Updated criteria for completion of safety follow-up after discontinuation and after SCT to include end of trial. e. Updated criteria for completion of safety follow-up after discontinuation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
05 October 2017	The FDA determined that the risks of pembrolizumab plus pomalidomide or lenalidomide outweighed any potential benefit for patients with multiple myeloma. Based on this decision, the treatment phase of KN183 and KN185 was closed effective immediately.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The MK-3475-185 study was stopped/terminated early. Endpoint statistics may be biased due to the incomplete treatment and follow-up of subjects after study termination.

Notes: