Clinical trial results:
An Open-Label, Randomized Phase 3 Trial of Combinations of Nivolumab, Pomalidomide and Dexamethasone in Relapsed and Refractory Multiple Myeloma

Summary

EudraCT number	2015-005699-21
Trial protocol	CZ AT SE DK NO ES PT DE GR PL IT
Global end of trial date	09 March 2022

Results information

Result version number	v1 (current)
This version publication date	16 March 2023
First version publication date	16 March 2023

Trial information

Trial identification

Sponsor protocol code	CA209-602

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02726581
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	11 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare progression free survival (PFS) between N-Pd and Pd arms, by investigator.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2016
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	Austria: 3
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Czechia: 31
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Israel: 21
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Portugal: 8
Country: Number of subjects enrolled	Puerto Rico: 1
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 55
Worldwide total number of subjects	170
EEA total number of subjects	81

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)	71
From 65 to 84 years	99
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study contains an exploratory third arm evaluating the clinical benefit and the safety of the combination therapy of elotuzumab, nivolumab, pomalidomide and dexamethasone (Arm C: NE-Pd). Participants randomized to the Pd arm were allowed to cross over to this exploratory NE-Pd arm at the time of progression.

Period 1

Period 1 title	Pre-Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: N-Pd

Arm description:

Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

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

Dosage and administration details:

4 mg PO QD

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

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

Dosage and administration details:

480 mg IV

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

240 mg IV

Arm title	Arm B: Pd

Arm description:

Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

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

Dosage and administration details:

4 mg PO QD

Arm title	Arm C: NE-Pd

Arm description:

Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Elotuzumab: - Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle - Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle - Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle Pomalidomide: 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: Days 1, 8, 15, and 22 of each cycle - Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks - Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab dosing weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg IV

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

Dosage and administration details:

480 mg IV

Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg IV

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg IV

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

Dosage and administration details:

4 mg PO QD

Number of subjects in period 1	Arm A: N-Pd	Arm B: Pd	Arm C: NE-Pd
Started	75	71	24
Completed	72	70	24
Not completed	3	1	0
Participant no longer meets study criteria	1	-	-
Administrative reason by sponsor	2	-	-
Participant request to discontinue study treatment	-	1	-

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: N-Pd

Arm description:

Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

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

Dosage and administration details:

240 mg IV

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

Dosage and administration details:

4 mg PO QD

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

Dosage and administration details:

480 mg IV

Arm title	Arm B: Pd

Arm description:

Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

Arm type	Experimental

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

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

Dosage and administration details:

4 mg PO QD

Arm title	Arm C: NE-Pd

Arm description:

Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Elotuzumab: - Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle - Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle - Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle Pomalidomide: 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: Days 1, 8, 15, and 22 of each cycle - Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks - Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab dosing weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg IV

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Participants </= 75years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle, Participants > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle

Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg IV

Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 20 mg/kg IV	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 480 mg IV	
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4 mg PO QD	

Number of subjects in period 2	Arm A: N-Pd	Arm B: Pd	Arm C: NE-Pd
Started	72	70	24
NE-Pd Crossover	0	8	0
Completed	0	0	0
Not completed	72	70	24
Adverse event, serious fatal	1	-	-
Disease progression	47	50	16
Participant withdrew consent	3	1	1
Study drug toxicity	6	3	2
Maximum clinical benefit	-	2	-
Participant no longer meets study criteria	-	1	-
Adverse event unrelated to study drug	4	4	2
Other reasons	9	8	2
Poor/non-compliance	1	-	-
Participant request to discontinue study treatment	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: N-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	
Reporting group title	Arm B: Pd
Reporting group description:	
Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	
Reporting group title	Arm C: NE-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Elotuzumab: - Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle - Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle - Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle Pomalidomide: 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: Days 1, 8, 15, and 22 of each cycle - Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks - Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab dosing weeks	

Reporting group values	Arm A: N-Pd	Arm B: Pd	Arm C: NE-Pd
Number of subjects	75	71	24
Age categorical Units: Subjects			
Adults (18-64 years)	32	29	10
From 65-84 years	43	42	14
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	65.9	65.5	66.2
standard deviation	± 9.4	± 8.7	± 11.5
Sex: Female, Male Units: Participants			
Female	24	25	8
Male	51	46	16
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	5	5
White	72	64	19
More than one race	0	0	0
Unknown or Not Reported	0	2	0
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	1	4	1
Not Hispanic or Latino	40	41	15
Unknown or Not Reported	34	26	8

Reporting group values	Total		
Number of subjects	170		
Age categorical Units: Subjects			
Adults (18-64 years)	71		
From 65-84 years	99		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	57		
Male	113		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	13		
White	155		
More than one race	0		
Unknown or Not Reported	2		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6		
Not Hispanic or Latino	96		
Unknown or Not Reported	68		

End points

End points reporting groups

Reporting group title	Arm A: N-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	

Reporting group title	Arm B: Pd
Reporting group description:	
Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	

Reporting group title	Arm C: NE-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Elotuzumab: - Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle - Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle - Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle Pomalidomide: 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: Days 1, 8, 15, and 22 of each cycle - Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks - Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab dosing weeks	

Reporting group title	Arm A: N-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	

Reporting group title	Arm B: Pd
Reporting group description:	
Pomalidomide: - 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: - Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle - Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle	

Reporting group title	Arm C: NE-Pd
Reporting group description:	
Nivolumab: - Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle - Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle Elotuzumab: - Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle - Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle - Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle Pomalidomide: 4 mg PO QD Days 1-21 of each 28-day cycle Dexamethasone: Days 1, 8, 15, and 22 of each cycle - Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks - Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab dosing weeks	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[1]
End point description:	
Randomization to first documented tumor progression or death due to any cause, whichever occurred first. Participants who die without reported prior progression are considered to have progressed on date of their death. Participants who did not progress or die will be censored at their last efficacy assessment. Participants who did not have on study efficacy assessments and alive will be censored on randomization date. Participants who started subsequent anti-cancer therapy without prior reported progression will be censored at last efficacy assessment prior to subsequent anti-cancer therapy. Progression is 1) increase of 25% from lowest confirmed response value in specific Serum M-protein and Urine M-protein criteria and increase of FLC for patients with no measurable M protein in blood or urine at baseline and/or 2)	

appearance of a new lesion(s), >/= 50% increase from nadir in SPD of > 1 lesion, or >/= 50% increase in the longest diameter of a previous lesion > 1 cm in short axis.

End point type	Primary

End point timeframe:

From randomization to the date of the first documented tumor progression or death due to any cause, whichever occurred first (Up to approximately 64 month)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This study contains an exploratory third arm not included in endpoint analysis.

End point values	Arm A: N-Pd	Arm B: Pd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	71		
Units: Months				
median (confidence interval 95%)	8.38 (5.78 to 12.06)	7.33 (6.47 to 8.44)		

Statistical analyses

Statistical analysis title	Summary of Progression-Free Survival
Comparison groups	Arm A: N-Pd v Arm B: Pd
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.3

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[2]

End point description:

The time between the date of randomization and the date of death due to any cause. OS will be censored on the last date a participant was known to be alive.

End point type	Secondary

End point timeframe:

From randomization to the date of death due to any cause (up to approximately 64 months)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This study contains an exploratory third arm not included in endpoint analysis.

End point values	Arm A: N-Pd	Arm B: Pd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	71		
Units: Months				
median (confidence interval 95%)	24.87 (15.61 to 34.40)	21.39 (17.91 to 27.56)		

Statistical analyses

Statistical analysis title	Summary of Overall Survival
Comparison groups	Arm A: N-Pd v Arm B: Pd
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.19

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[3]

End point description:

The percentage of randomized participants who achieved a best overall response (BOR) of stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) using International Myeloma Working Group (IMWG) criteria.

sCR= Complete response as defined below plus normal FLC ratio and absence of clonal cells in bone marrow biopsy by immunohistochemistry.
CR = Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and < 5% plasma cells in bone marrow aspirates.
VGPR = Serum and urine M-protein detectable by immunofixation but not on electrophoresis or >/= 90% reduction in serum M-protein plus urine M-protein level < 100 mg per 24 h.
PR = >/= 50% reduction of serum M-protein plus reduction in 24 h urinary M-protein by >/= 90% or to < 200 mg per 24 h.

End point type	Secondary

End point timeframe:

From randomization up to approximately 64 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This study contains an exploratory third arm not included in endpoint analysis.

End point values	Arm A: N-Pd	Arm B: Pd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	71		
Units: Percentage of participants				
number (confidence interval 95%)	48.0 (36.3 to 59.8)	54.9 (42.7 to 66.8)		

Statistical analyses

Statistical analysis title	Summary Objective Response Rate
Comparison groups	Arm A: N-Pd v Arm B: Pd
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.46

Secondary: Time to Objective Response (TTR)

End point title	Time to Objective Response (TTR)[4]

End point description:

The time from the date of randomization to the date of the first stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR).

sCR= Complete response as defined below plus normal FLC ratio and absence of clonal cells in bone marrow biopsy by immunohistochemistry.
CR = Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and < 5% plasma cells in bone marrow aspirates.
VGPR = Serum and urine M-protein detectable by immunofixation but not on electrophoresis or >/= 90% reduction in serum M-protein plus urine M-protein level < 100 mg per 24 h.
PR = >/= 50% reduction of serum M-protein plus reduction in 24 h urinary M-protein by >/= 90% or to < 200 mg per 24 h.

End point type	Secondary

End point timeframe:

From the date of randomization to the date of the first sCR, CR, VGPR, or PR (up to approximately 64 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This study contains an exploratory third arm not included in endpoint analysis.

End point values	Arm A: N-Pd	Arm B: Pd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	39		
Units: Months				
arithmetic mean (standard deviation)	5.91 (± 9.09)	4.37 (± 5.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR)

End point title	Duration of Objective Response (DOR)[5]

End point description:

The time between the date of first response to the date of the first objectively documented tumor progression as assessed by the investigator according to International Myeloma Working Group (IMWG) criteria or death due to any cause prior to subsequent anti-cancer therapy. Participants who neither progress nor die will be censored on the date of their last tumor assessment prior to subsequent anti-cancer therapy. Progression is 1) increase of 25% from lowest confirmed response value in specific Serum M-protein and Urine M-protein criteria and increase of FLC for patients with no measurable M protein in blood or urine at baseline and/or 2) appearance of a new lesion(s), >/= 50% increase from nadir in SPD of > 1 lesion, or >/= 50% increase in the longest diameter of a previous lesion > 1 cm in short axis.

End point type	Secondary

End point timeframe:

From randomization to the date of the first objectively documented tumor progression or death due to any cause prior to subsequent anti-cancer therapy (up to approximately 64 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This study contains an exploratory third arm not included in endpoint analysis.

End point values	Arm A: N-Pd	Arm B: Pd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	39		
Units: Months				
median (confidence interval 95%)	8.51 (6.47 to 13.83)	6.47 (5.55 to 11.07)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/NSAEs assessed from first dose to 100 days post last dose (up to approximately 63 months) Participants were assessed for all-cause mortality from their randomization to the study's Primary completion (up to approximately 64 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Arm A: N-Pd

Reporting group description:

Nivolumab:
- Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle.
- Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle.

Pomalidomide:
- 4 mg PO QD Days 1-21 of each 28-day cycle.

Dexamethasone:
- Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle
- Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle.

Reporting group title	Arm B: NE-Pd Crossover

Reporting group description:

Participants who progressed on the Pd
control arm and were allowed to crossover to the NE-Pd exploratory arm.

Reporting group title	Arm C: NE-Pd

Reporting group description:

Nivolumab:
- Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28-day cycle.
- Cycles 5 and beyond: 480 mg IV Day 1 of each 28-day cycle.

Elotuzumab:
- Cycles 1 - 2: 10 mg/kg IV Days 1, 8, 15, and 22 of each 28-day cycle.
- Cycle 3 and 4: 10mg/kg IV Day 1 and 15 of each 28-day cycle.
- Cycles 5 and beyond: 20 mg/kg IV Day 1 of each 28-day cycle.

Pomalidomide:
4 mg PO QD Days 1-21 of each 28-day cycle.

Dexamethasone:
Days 1, 8, 15, and 22 of each cycle.
- Subjects </= 75 years old: weeks with elotuzumab dosing: 28 mg PO + 8 mg IV and 40 mg PO on non-elotuzumab dosing weeks.
- Subjects > 75 years old: weeks with elotuzumab dosing: 8 mg PO + 8 mg IV and 20 mg PO on non-elotuzumab
dosing weeks.

Reporting group title	Arm B: Pd

Reporting group description:

Pomalidomide:
- 4 mg PO QD Days 1-21 of each 28-day cycle.

Dexamethasone:
- Subjects </= 75 years old: 40 mg PO Days (1, 8, 15, and 22) of each cycle
- Subjects > 75 years old: 20 mg PO Days (1, 8, 15, and 22) of each cycle.

Serious adverse events	Arm A: N-Pd	Arm B: NE-Pd Crossover	Arm C: NE-Pd
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 72 (72.22%)	5 / 8 (62.50%)	18 / 24 (75.00%)
number of deaths (all causes)	47	5	17
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal neoplasm			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung cancer metastatic			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	9 / 72 (12.50%)	2 / 8 (25.00%)	4 / 24 (16.67%)
occurrences causally related to treatment / all	0 / 9	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 8	0 / 2	0 / 4
Plasma cell leukaemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Plasma cell myeloma			

subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Plasmacytoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal neoplasm			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Refractory cytopenia with unilineage dysplasia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			

subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			

subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	3 / 5	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 72 (2.78%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	2 / 2	1 / 1	3 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 72 (2.78%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lower limb fracture			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			

subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block first degree			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial nerve disorder			

subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vomiting			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute kidney injury			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	4 / 24 (16.67%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hydronephrosis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Arthritis bacterial			

subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	3 / 24 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			

subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	9 / 72 (12.50%)	0 / 8 (0.00%)	6 / 24 (25.00%)
occurrences causally related to treatment / all	4 / 10	0 / 0	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia staphylococcal			

subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia fungal			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	8 / 72 (11.11%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences causally related to treatment / all	2 / 8	1 / 1	2 / 3
deaths causally related to treatment / all	1 / 5	0 / 0	0 / 1
Septic shock			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			

subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm B: Pd		
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 70 (58.57%)		
number of deaths (all causes)	49		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal neoplasm			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myeloid leukaemia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung cancer metastatic			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 6		

Plasma cell leukaemia				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cell myeloma				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Plasmacytoma				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal neoplasm				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Refractory cytopenia with unilineage dysplasia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Deep vein thrombosis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haematoma				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Condition aggravated				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Non-cardiac chest pain				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised oedema				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 70 (5.71%)			
occurrences causally related to treatment / all	4 / 6			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypogammaglobulinaemia				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Atelectasis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Dyspnoea exertional			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Confusional state				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood glucose increased				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin laceration				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Humerus fracture				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural complication				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrioventricular block complete				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Cardiac arrest				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block first degree				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Encephalopathy				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral thrombosis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysarthria				

subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial nerve disorder				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lacunar stroke				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tremor				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				

subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Incarcerated inguinal hernia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				

subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus viraemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parainfluenzae virus infection				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Herpes simplex				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand-foot-and-mouth disease				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii infection				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	17 / 70 (24.29%)			
occurrences causally related to treatment / all	8 / 20			
deaths causally related to treatment / all	0 / 1			
Pneumonia cytomegaloviral				

subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia legionella				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia parainfluenzae viral				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia fungal				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				

subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	3 / 70 (4.29%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	3 / 70 (4.29%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Staphylococcal bacteraemia				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hypoglycaemia				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Electrolyte imbalance				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fluid retention				
subjects affected / exposed	0 / 70 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				

subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: N-Pd	Arm B: NE-Pd Crossover	Arm C: NE-Pd
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 72 (97.22%)	7 / 8 (87.50%)	24 / 24 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	5	0	2
Haematoma			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Embolism			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Aortic stenosis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	3	1	4
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	34 / 72 (47.22%)	6 / 8 (75.00%)	10 / 24 (41.67%)
occurrences (all)	44	6	11
Chills			
subjects affected / exposed	2 / 72 (2.78%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	5	1	0
Chest pain			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Asthenia			
subjects affected / exposed	15 / 72 (20.83%)	2 / 8 (25.00%)	4 / 24 (16.67%)
occurrences (all)	18	2	4
Non-cardiac chest pain			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	5	0	0
Pyrexia			
subjects affected / exposed	10 / 72 (13.89%)	1 / 8 (12.50%)	14 / 24 (58.33%)
occurrences (all)	16	3	28
Pain			
subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	1	1	1
Oedema peripheral			
subjects affected / exposed	14 / 72 (19.44%)	1 / 8 (12.50%)	7 / 24 (29.17%)
occurrences (all)	17	1	7
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			

subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Productive cough			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	4	0	1
Pneumonitis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	1	1	4
Cough			
subjects affected / exposed	11 / 72 (15.28%)	0 / 8 (0.00%)	6 / 24 (25.00%)
occurrences (all)	20	0	8
Dysphonia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	13 / 72 (18.06%)	2 / 8 (25.00%)	6 / 24 (25.00%)
occurrences (all)	19	2	8
Epistaxis			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	3 / 24 (12.50%)
occurrences (all)	4	0	3
Hypoxia			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	3	0	2
Nasal congestion			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 72 (15.28%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	11	0	1
Anxiety			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	2	0	2
Confusional state			
subjects affected / exposed	5 / 72 (6.94%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	6	1	3

Hallucination			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Investigations			
White blood cell count decreased			
subjects affected / exposed	6 / 72 (8.33%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	13	0	4
Weight decreased			
subjects affected / exposed	4 / 72 (5.56%)	2 / 8 (25.00%)	3 / 24 (12.50%)
occurrences (all)	5	2	6
Platelet count decreased			
subjects affected / exposed	5 / 72 (6.94%)	1 / 8 (12.50%)	4 / 24 (16.67%)
occurrences (all)	8	1	4
Neutrophil count decreased			
subjects affected / exposed	7 / 72 (9.72%)	0 / 8 (0.00%)	3 / 24 (12.50%)
occurrences (all)	16	0	10
Lymphocyte count decreased			
subjects affected / exposed	7 / 72 (9.72%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	14	0	3
Blood creatinine increased			
subjects affected / exposed	8 / 72 (11.11%)	0 / 8 (0.00%)	3 / 24 (12.50%)
occurrences (all)	13	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Alanine aminotransferase increased			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	2	0	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	4 / 24 (16.67%)
occurrences (all)	3	2	4
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	1	1	0

Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 72 (11.11%)	0 / 8 (0.00%)	7 / 24 (29.17%)
occurrences (all)	8	0	11
Headache			
subjects affected / exposed	7 / 72 (9.72%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	10	1	3
Hypoaesthesia			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	3	1	1
Neuropathy peripheral			
subjects affected / exposed	2 / 72 (2.78%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	2	1	2
Paraesthesia			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	5	0	1
Tremor			
subjects affected / exposed	8 / 72 (11.11%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	8	0	2
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 72 (5.56%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	4	2	3
Lymphopenia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	0	1	2
Neutropenia			
subjects affected / exposed	24 / 72 (33.33%)	0 / 8 (0.00%)	10 / 24 (41.67%)
occurrences (all)	68	0	16
Thrombocytopenia			
subjects affected / exposed	16 / 72 (22.22%)	0 / 8 (0.00%)	4 / 24 (16.67%)
occurrences (all)	30	0	5
Pancytopenia			

subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	26 / 72 (36.11%)	2 / 8 (25.00%)	11 / 24 (45.83%)
occurrences (all)	38	2	14
Eye disorders			
Vitreous detachment			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	4	0	0
Vision blurred			
subjects affected / exposed	10 / 72 (13.89%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	11	1	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	2	0	1
Abdominal pain			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	6	0	1
Constipation			
subjects affected / exposed	17 / 72 (23.61%)	0 / 8 (0.00%)	4 / 24 (16.67%)
occurrences (all)	20	0	4
Diarrhoea			
subjects affected / exposed	22 / 72 (30.56%)	2 / 8 (25.00%)	5 / 24 (20.83%)
occurrences (all)	29	2	6
Dry mouth			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	3	1	1
Dyspepsia			

subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	5	0	1
Dysphagia			
subjects affected / exposed	2 / 72 (2.78%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	2	1	1
Nausea			
subjects affected / exposed	14 / 72 (19.44%)	2 / 8 (25.00%)	4 / 24 (16.67%)
occurrences (all)	15	2	4
Vomiting			
subjects affected / exposed	5 / 72 (6.94%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	7	2	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	4	0	2
Alopecia			
subjects affected / exposed	1 / 72 (1.39%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	11 / 72 (15.28%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	13	1	4
Pruritus			
subjects affected / exposed	9 / 72 (12.50%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	10	0	2
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 72 (0.00%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Chronic kidney disease			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	4	0	2
Hyperthyroidism			
subjects affected / exposed	2 / 72 (2.78%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	2	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 72 (15.28%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	11	1	0
Back pain			
subjects affected / exposed	12 / 72 (16.67%)	1 / 8 (12.50%)	4 / 24 (16.67%)
occurrences (all)	15	1	4
Bone pain			
subjects affected / exposed	7 / 72 (9.72%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	8	1	0
Muscle spasms			
subjects affected / exposed	6 / 72 (8.33%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	6	1	3
Muscular weakness			
subjects affected / exposed	6 / 72 (8.33%)	0 / 8 (0.00%)	5 / 24 (20.83%)
occurrences (all)	6	0	5
Neck pain			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal chest pain			
subjects affected / exposed	6 / 72 (8.33%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	6	1	2
Pain in extremity			
subjects affected / exposed	7 / 72 (9.72%)	1 / 8 (12.50%)	2 / 24 (8.33%)
occurrences (all)	7	1	2
Resorption bone increased			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Myalgia			

subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	4	0	1
Infections and infestations			
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Oral infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	5 / 72 (6.94%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	5	0	0
Influenza			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	3	0	2
Escherichia urinary tract infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	8 / 72 (11.11%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	10	0	1
Pneumonia			
subjects affected / exposed	10 / 72 (13.89%)	0 / 8 (0.00%)	5 / 24 (20.83%)
occurrences (all)	13	0	5
Sinusitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	4 / 24 (16.67%)
occurrences (all)	1	0	4
Urinary tract infection			
subjects affected / exposed	7 / 72 (9.72%)	0 / 8 (0.00%)	1 / 24 (4.17%)
occurrences (all)	10	0	3
Upper respiratory tract infection			
subjects affected / exposed	14 / 72 (19.44%)	0 / 8 (0.00%)	3 / 24 (12.50%)
occurrences (all)	22	0	5

Respiratory tract infection			
subjects affected / exposed	9 / 72 (12.50%)	0 / 8 (0.00%)	0 / 24 (0.00%)
occurrences (all)	13	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 72 (16.67%)	2 / 8 (25.00%)	2 / 24 (8.33%)
occurrences (all)	13	2	2
Dehydration			
subjects affected / exposed	4 / 72 (5.56%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	4	0	2
Hypercalcaemia			
subjects affected / exposed	7 / 72 (9.72%)	2 / 8 (25.00%)	0 / 24 (0.00%)
occurrences (all)	12	3	0
Hyperglycaemia			
subjects affected / exposed	3 / 72 (4.17%)	0 / 8 (0.00%)	4 / 24 (16.67%)
occurrences (all)	8	0	4
Hyperkalaemia			
subjects affected / exposed	2 / 72 (2.78%)	2 / 8 (25.00%)	1 / 24 (4.17%)
occurrences (all)	2	3	2
Hyperuricaemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 8 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	3
Hypocalcaemia			
subjects affected / exposed	5 / 72 (6.94%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	6	1	3
Hypokalaemia			
subjects affected / exposed	5 / 72 (6.94%)	1 / 8 (12.50%)	4 / 24 (16.67%)
occurrences (all)	6	1	6
Hypomagnesaemia			
subjects affected / exposed	9 / 72 (12.50%)	2 / 8 (25.00%)	5 / 24 (20.83%)
occurrences (all)	14	2	5
Hyponatraemia			
subjects affected / exposed	3 / 72 (4.17%)	1 / 8 (12.50%)	3 / 24 (12.50%)
occurrences (all)	6	1	3
Hypophosphataemia			

subjects affected / exposed	4 / 72 (5.56%)	1 / 8 (12.50%)	1 / 24 (4.17%)
occurrences (all)	4	1	2
Vitamin B1 deficiency			
subjects affected / exposed	0 / 72 (0.00%)	1 / 8 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Arm B: Pd		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 70 (92.86%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 70 (12.86%)		
occurrences (all)	9		
Haematoma			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Embolism			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Aortic stenosis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	24 / 70 (34.29%)		
occurrences (all)	28		
Chills			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	5		
Chest pain			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Asthenia			

subjects affected / exposed	12 / 70 (17.14%)		
occurrences (all)	12		
Non-cardiac chest pain			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	9 / 70 (12.86%)		
occurrences (all)	21		
Pain			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	15 / 70 (21.43%)		
occurrences (all)	17		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	5		
Pulmonary embolism			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Pneumonitis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	12 / 70 (17.14%)		
occurrences (all)	15		
Dysphonia			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	15 / 70 (21.43%)		
occurrences (all)	20		
Epistaxis			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Hypoxia			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	5		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	11		
Anxiety			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	6		
Confusional state			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	7		
Hallucination			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Investigations			
White blood cell count decreased			
subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	17		
Weight decreased			

subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	9		
Neutrophil count decreased			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	19		
Lymphocyte count decreased			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	10		
Blood creatinine increased			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	5		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	4		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 70 (14.29%)		
occurrences (all)	15		
Headache			
subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	7		
Hypoaesthesia			

subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Neuropathy peripheral			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	7		
Paraesthesia			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Lymphopenia			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	22 / 70 (31.43%)		
occurrences (all)	46		
Thrombocytopenia			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	17		
Pancytopenia			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	20 / 70 (28.57%)		
occurrences (all)	25		
Eye disorders			
Vitreous detachment			

subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Vision blurred			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Abdominal pain			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	7		
Abdominal pain upper			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	15 / 70 (21.43%)		
occurrences (all)	20		
Diarrhoea			
subjects affected / exposed	17 / 70 (24.29%)		
occurrences (all)	21		
Dry mouth			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Dyspepsia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	17		

Vomiting subjects affected / exposed occurrences (all)	6 / 70 (8.57%) 8		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 0 / 70 (0.00%) 0 1 / 70 (1.43%) 1 8 / 70 (11.43%) 9 4 / 70 (5.71%) 4		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) Urinary incontinence subjects affected / exposed occurrences (all) Chronic kidney disease subjects affected / exposed occurrences (all)	 1 / 70 (1.43%) 1 0 / 70 (0.00%) 0 4 / 70 (5.71%) 4		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all)	 0 / 70 (0.00%) 0 1 / 70 (1.43%) 1		
Musculoskeletal and connective tissue disorders Arthralgia			

subjects affected / exposed	8 / 70 (11.43%)		
occurrences (all)	9		
Back pain			
subjects affected / exposed	15 / 70 (21.43%)		
occurrences (all)	18		
Bone pain			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	6		
Muscle spasms			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	15		
Muscular weakness			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Neck pain			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	4		
Resorption bone increased			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Infections and infestations			
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Oral infection			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		

Nasopharyngitis			
subjects affected / exposed	12 / 70 (17.14%)		
occurrences (all)	12		
Influenza			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	6		
Pneumonia			
subjects affected / exposed	12 / 70 (17.14%)		
occurrences (all)	13		
Sinusitis			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	22 / 70 (31.43%)		
occurrences (all)	26		
Respiratory tract infection			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	6		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 70 (14.29%)		
occurrences (all)	10		
Dehydration			

subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Hyperglycaemia			
subjects affected / exposed	10 / 70 (14.29%)		
occurrences (all)	19		
Hyperkalaemia			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Hyperuricaemia			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	4		
Hypokalaemia			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	7		
Hypomagnesaemia			
subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	12		
Hyponatraemia			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	4		
Hypophosphataemia			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Vitamin B1 deficiency			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2018	Incorporates changes required by the FDA per the partial clinical hold based on safety concerns from pembrolizumab studies, as well as study design and objective changes to reflect endpoints adequacy in light of these safety concerns. Incorporates new biomarker collections which align with the BMS multiple myeloma program level approach. Revision of efficacy assessments (Appendix III) to align with the current International Myeloma Working Group (IMWG) guidance.
12 November 2018	Enrollment into the study was stopped as of 23-August-2018. All efficacy assessments will be based on the investigator evaluation rather than Independent Review Committee (IRC). Bone marrow aspirate collection time-points and samples are reduced. Pharmacokinetic (PK), immunogenicity/antidrug-antibody (ADA) collections and quality of life (QOL) evaluations are cancelled. Update of Appendix 3 Definitions of Response and Progression criteria, Appendix 5 Nivolumab Management Algorithm and Appendix 6 Pomalidomide Pregnancy Risk Prevention Plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to the early enrolment termination to Study CA209602 and the smaller than planned study sample size, the statistical analyses were not sufficiently powered.

Notes: