



Clinical trial results:

An Open Label, Randomized Phase 2 Trial of Pomalidomide/Dexamethasone With or Without Elotuzumab in relapsed and refractory Multiple Myeloma.

Summary

EudraCT number	2014-003282-19
Trial protocol	NL ES DE GR FR PL IT
Global end of trial date	21 October 2021

Results information

Result version number	v1 (current)
This version publication date	21 October 2022
First version publication date	21 October 2022

Trial information

Trial identification

Sponsor protocol code	CA204-125
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	10 December 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare progression free survival (PFS) between treatment arms

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	18 March 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	Canada: 5
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Greece: 23
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	117
EEA total number of subjects	87

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)	44
From 65 to 84 years	73
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

117 participants were randomized, and 115 participants were treated.

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	E-Pd Cohort

Arm description:

Elotuzumab + Pomalidomide + Dexamethasone

Arm type	Experimental
Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cycle 1 and 2: 10 mg/kg IV on Days 1, 8, 15, and 22 of each cycle (1 cycle = 28 days).

Cycle 3 and beyond: 20 mg/Kg IV Day 1 of each cycle

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

Dosage and administration details:

Subjects ≤ 75 years old: 40 mg PO per day (days 1, 8, 15, and 22 of each cycle).

Subjects > 75 years old: 20 mg PO per day (days 1, 8, 15, and 22 of each cycle).

1 cycle=28 days

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

Dosage and administration details:

4 mg PO daily (Days 1-21) of each cycle (1 cycle = 28 days).

Arm title	Pd Cohort
Arm description:	
Pomalidomide + Dexamethasone	
Arm type	Experimental

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

Dosage and administration details:

Subjects ≤ 75 years old: 40 mg PO per day (days 1, 8, 15, and 22 of each cycle).

Subjects > 75 years old: 20 mg PO per day (days 1, 8, 15, and 22 of each cycle).

1 cycle=28 days

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

Dosage and administration details:

4 mg PO daily (Days 1-21) of each cycle (1 cycle = 28 days).

Number of subjects in period 1	E-Pd Cohort	Pd Cohort
Started	60	57
Completed	60	55
Not completed	0	2
Participant Withdrew Consent	-	2

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	E-Pd Cohort

Arm description:

Elotuzumab + Pomalidomide + Dexamethasone

Arm type	Experimental
Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cycle 1 and 2: 10 mg/kg IV on Days 1, 8, 15, and 22 of each cycle (1 cycle = 28 days). Cycle 3 and beyond: 20 mg/Kg IV Day 1 of each cycle

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

Dosage and administration details:

Subjects ≤ 75 years old: 40 mg PO per day (days 1, 8, 15, and 22 of each cycle). Subjects > 75 years old: 20 mg PO per day (days 1, 8, 15, and 22 of each cycle). 1 cycle=28 days

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

Dosage and administration details:

4 mg PO daily (Days 1-21) of each cycle (1 cycle = 28 days).

Arm title	Pd Cohort
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Arm description:

Pomalidomide + Dexamethasone

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

Dosage and administration details:

Subjects ≤ 75 years old: 40 mg PO per day (days 1, 8, 15, and 22 of each cycle). Subjects > 75 years old: 20 mg PO per day (days 1, 8, 15, and 22 of each cycle). 1 cycle=28 days

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

Dosage and administration details:

4 mg PO daily (Days 1-21) of each cycle (1 cycle = 28 days).

Number of subjects in period 2	E-Pd Cohort	Pd Cohort
Started	60	55
Completed	0	0
Not completed	60	55
Adverse event, serious fatal	1	-
Consent withdrawn by subject	2	1
Disease progression	43	38
Adverse Event unrelated to study drug	6	9
Study drug toxicity	2	2
Participant request to discontinue	2	-
Maximum Clinical Benefit	-	2

Other reasons	4	2
Administrative reasons by sponsor	-	1

Baseline characteristics

Reporting groups

Reporting group title	E-Pd Cohort
Reporting group description: Elotuzumab + Pomalidomide + Dexamethasone	
Reporting group title	Pd Cohort
Reporting group description: Pomalidomide + Dexamethasone	

Reporting group values	E-Pd Cohort	Pd Cohort	Total
Number of subjects	60	57	117
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	22	22	44
>=65 years	38	35	73
Age Continuous Units: Years			
arithmetic mean	66.2	65.5	-
standard deviation	± 9.92	± 9.95	
Sex: Female, Male Units: Participants			
Female	28	22	50
Male	32	35	67
Race/Ethnicity, Customized Units: Subjects			
White	45	45	90
Black or African American	0	1	1
Asian	15	9	24
Other	0	2	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	10	18	28
Unknown or Not Reported	49	39	88

End points

End points reporting groups

Reporting group title	E-Pd Cohort
Reporting group description: Elotuzumab + Pomalidomide + Dexamethasone	
Reporting group title	Pd Cohort
Reporting group description: Pomalidomide + Dexamethasone	
Reporting group title	E-Pd Cohort
Reporting group description: Elotuzumab + Pomalidomide + Dexamethasone	
Reporting group title	Pd Cohort
Reporting group description: Pomalidomide + Dexamethasone	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description: PFS is defined as the time from randomization to the date of the first documented tumor progression or death due to any cause. Progressive disease response criteria were defined as an increase of 25% from lowest response value in any one or more of the following: 1. Serum M-component and/or 2. Urine M-component and/or 3. Only in patients without measurable serum and urine M-protein levels: the difference between involved and uninvolved FLC levels 4. Bone marrow plasma cell percentage; Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas; Development of hypercalcemia that can be attributed solely to the plasma cell proliferative disorder. 9999=NA	
End point type	Primary
End point timeframe: From randomization to date of progression or death (up to approximately 21 months)	

End point values	E-Pd Cohort	Pd Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Months				
median (confidence interval 95%)	10.25 (6.54 to 9999)	4.70 (2.83 to 7.62)		

Statistical analyses

Statistical analysis title	PFS
Comparison groups	E-Pd Cohort v Pd Cohort

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0043
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.82

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
<p>ORR is defined as the percentage of 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 the modified International Myeloma Working Group (IMWG) criteria described as follows, as per investigator's assessment</p> <ul style="list-style-type: none"> - CR: Negative immunofixation of serum and urine and disappearance of any soft tissue plasmacytomas, and < 5% plasma cells in bone marrow - sCR: CR, as defined above, plus the following: Normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence - VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or $\geq 90\%$ reduction in serum M-protein level plus urine M-protein level < 100 mg per 24 hour - PR: $\geq 50\%$ reduction of serum M-protein and reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg per 24 hour. 	
End point type	Secondary
End point timeframe:	
From first dose to disease progression (up to approximately 21 months)	

End point values	E-Pd Cohort	Pd Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Percent of participants				
number (confidence interval 95%)	58.3 (44.9 to 70.9)	24.6 (14.1 to 37.8)		

Statistical analyses

Statistical analysis title	ORR
Comparison groups	E-Pd Cohort v Pd Cohort

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	10.43

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS is the time from randomization to the date of death from any cause. The survival time for participants who had not died was censored at the last known alive date. OS was censored at the date of randomization for subjects who were randomized but had no follow-up.	
End point type	Secondary
End point timeframe:	
From randomization to death (up to approximately 52 months)	

End point values	E-Pd Cohort	Pd Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Months				
median (confidence interval 95%)	29.80 (22.87 to 45.67)	17.41 (13.83 to 27.70)		

Statistical analyses

Statistical analysis title	OS Analysis
Comparison groups	E-Pd Cohort v Pd Cohort
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0217
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.93

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: from randomization to study completion (up to approximately 67 months)

SAEs and Other Adverse Events: from first dose to 60 days following last dose (up to approximately 60 months)

Adverse event reporting additional description:

All-cause mortality: all randomized participants

SAEs and Other Adverse Events: all treated participants

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	E-Pd Cohort
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Reporting group description:

Elotuzumab + Pomalidomide + Dexamethasone

Reporting group title	Pd Cohort
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Reporting group description:

Pomalidomide + Dexamethasone

Serious adverse events	E-Pd Cohort	Pd Cohort	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 60 (70.00%)	33 / 55 (60.00%)	
number of deaths (all causes)	41	41	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 60 (1.67%)	7 / 55 (12.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 5	
Lung neoplasm malignant			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Invasive breast carcinoma			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Metastases to bone			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage II			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell leukaemia			
subjects affected / exposed	0 / 60 (0.00%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
General physical health deterioration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

Non-cardiac chest pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Primary amyloidosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			

subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 60 (0.00%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	3 / 60 (5.00%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	3 / 60 (5.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract subcapsular			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 60 (3.33%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder prolapse			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal failure			
subjects affected / exposed	0 / 60 (0.00%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Escherichia sepsis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 60 (5.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 60 (6.67%)	5 / 55 (9.09%)	
occurrences causally related to treatment / all	3 / 5	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia influenzal			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			

subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 60 (3.33%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 2	1 / 2	
Sepsis			
subjects affected / exposed	1 / 60 (1.67%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	5 / 60 (8.33%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			

subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 60 (1.67%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	E-Pd Cohort	Pd Cohort	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 60 (93.33%)	49 / 55 (89.09%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 60 (5.00%)	3 / 55 (5.45%)	
occurrences (all)	3	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 60 (13.33%)	5 / 55 (9.09%)	
occurrences (all)	12	5	
Pyrexia			
subjects affected / exposed	11 / 60 (18.33%)	12 / 55 (21.82%)	
occurrences (all)	19	15	
Oedema peripheral			
subjects affected / exposed	11 / 60 (18.33%)	5 / 55 (9.09%)	
occurrences (all)	14	7	
Fatigue			
subjects affected / exposed	11 / 60 (18.33%)	8 / 55 (14.55%)	
occurrences (all)	11	9	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 60 (8.33%)	5 / 55 (9.09%)	
occurrences (all)	10	7	
Dyspnoea			
subjects affected / exposed	9 / 60 (15.00%)	4 / 55 (7.27%)	
occurrences (all)	9	4	
Productive cough			
subjects affected / exposed	4 / 60 (6.67%)	4 / 55 (7.27%)	
occurrences (all)	4	4	
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 60 (6.67%)	2 / 55 (3.64%)	
occurrences (all)	4	2	
Insomnia			
subjects affected / exposed	10 / 60 (16.67%)	7 / 55 (12.73%)	
occurrences (all)	11	8	
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 60 (6.67%)	6 / 55 (10.91%)	
occurrences (all)	4	6	
Neutrophil count decreased			
subjects affected / exposed	4 / 60 (6.67%)	5 / 55 (9.09%)	
occurrences (all)	5	8	
White blood cell count decreased			
subjects affected / exposed	2 / 60 (3.33%)	3 / 55 (5.45%)	
occurrences (all)	2	3	
Platelet count decreased			
subjects affected / exposed	4 / 60 (6.67%)	4 / 55 (7.27%)	
occurrences (all)	4	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 60 (3.33%)	3 / 55 (5.45%)	
occurrences (all)	2	5	
Hypoaesthesia			

subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	1 / 55 (1.82%) 1	
Neuropathy peripheral subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	3 / 55 (5.45%) 3	
Polyneuropathy subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	1 / 55 (1.82%) 1	
Tremor subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 55 (3.64%) 3	
Blood and lymphatic system disorders			
Lymphopenia subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 10	1 / 55 (1.82%) 1	
Anaemia subjects affected / exposed occurrences (all)	17 / 60 (28.33%) 29	21 / 55 (38.18%) 30	
Leukopenia subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 17	4 / 55 (7.27%) 4	
Neutropenia subjects affected / exposed occurrences (all)	16 / 60 (26.67%) 27	17 / 55 (30.91%) 27	
Thrombocytopenia subjects affected / exposed occurrences (all)	9 / 60 (15.00%) 10	11 / 55 (20.00%) 13	
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 6	0 / 55 (0.00%) 0	
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	4 / 55 (7.27%) 4	
Constipation			

subjects affected / exposed occurrences (all)	14 / 60 (23.33%) 18	6 / 55 (10.91%) 7	
Stomatitis subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	1 / 55 (1.82%) 1	
Nausea subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	5 / 55 (9.09%) 6	
Diarrhoea subjects affected / exposed occurrences (all)	15 / 60 (25.00%) 22	7 / 55 (12.73%) 9	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 9	6 / 55 (10.91%) 6	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	7 / 55 (12.73%) 7	
Back pain subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 7	5 / 55 (9.09%) 5	
Bone pain subjects affected / exposed occurrences (all)	11 / 60 (18.33%) 15	5 / 55 (9.09%) 6	
Pain in extremity subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	3 / 55 (5.45%) 3	
Muscular weakness subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	4 / 55 (7.27%) 5	
Muscle spasms subjects affected / exposed occurrences (all)	9 / 60 (15.00%) 12	4 / 55 (7.27%) 4	
Infections and infestations			

Influenza			
subjects affected / exposed	4 / 60 (6.67%)	4 / 55 (7.27%)	
occurrences (all)	5	5	
Bronchitis			
subjects affected / exposed	9 / 60 (15.00%)	5 / 55 (9.09%)	
occurrences (all)	12	6	
Respiratory tract infection			
subjects affected / exposed	10 / 60 (16.67%)	5 / 55 (9.09%)	
occurrences (all)	13	7	
Pneumonia			
subjects affected / exposed	4 / 60 (6.67%)	3 / 55 (5.45%)	
occurrences (all)	5	3	
Pharyngitis			
subjects affected / exposed	5 / 60 (8.33%)	1 / 55 (1.82%)	
occurrences (all)	5	1	
Oral candidiasis			
subjects affected / exposed	1 / 60 (1.67%)	3 / 55 (5.45%)	
occurrences (all)	2	3	
Upper respiratory tract infection			
subjects affected / exposed	8 / 60 (13.33%)	9 / 55 (16.36%)	
occurrences (all)	11	11	
Nasopharyngitis			
subjects affected / exposed	15 / 60 (25.00%)	9 / 55 (16.36%)	
occurrences (all)	22	14	
Urinary tract infection			
subjects affected / exposed	5 / 60 (8.33%)	3 / 55 (5.45%)	
occurrences (all)	6	4	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	13 / 60 (21.67%)	11 / 55 (20.00%)	
occurrences (all)	17	13	
Hypercalcaemia			
subjects affected / exposed	3 / 60 (5.00%)	5 / 55 (9.09%)	
occurrences (all)	3	7	
Decreased appetite			

subjects affected / exposed	6 / 60 (10.00%)	4 / 55 (7.27%)	
occurrences (all)	6	6	
Hypokalaemia			
subjects affected / exposed	7 / 60 (11.67%)	7 / 55 (12.73%)	
occurrences (all)	9	9	
Hypomagnesaemia			
subjects affected / exposed	5 / 60 (8.33%)	3 / 55 (5.45%)	
occurrences (all)	6	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2015	Updates to risk management programs
12 February 2020	Updates on OS statistical considerations. Updates on assessment for efficacy analyses

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported