



Clinical trial results:

A Phase 2, Randomized Study of Bortezomib/Dexamethasone With or Without Elotuzumab in subjects with Relapsed/Refractory Multiple Myeloma

Summary

EudraCT number	2011-002695-16
Trial protocol	ES IT
Global end of trial date	21 April 2017

Results information

Result version number	v1 (current)
This version publication date	06 May 2018
First version publication date	06 May 2018

Trial information

Trial identification

Sponsor protocol code	ca204-009
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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	21 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of study CA204-009 was to evaluate the effect of elotuzumab in combination with bortezomib and dexamethasone, (E-Bd; investigational arm) compared with bortezomib and dexamethasone alone (Bd; control group) in subjects with relapsed/refractory multiple myeloma.

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Italy: 75
Country: Number of subjects enrolled	United States: 61
Worldwide total number of subjects	185
EEA total number of subjects	124

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)	83

From 65 to 84 years	101
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

185 subjects were enrolled, 152 subjects were randomized. Reasons not randomized: 23 no longer met study criteria, 5 withdrew consent, 2 died, 3 had poor/non-compliance. 150 were treated with study drug. 2 subjects were not treated: 1 withdrawal by subject and 1 physician decision.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Elotuzumab + Bortezomib + Dexamethasone

Arm description:

Elotuzumab: Solution; Intravenous (IV); 10 mg/kg; (Cycles 1 & 2: Days 1, 8 & 15; Cycles 3-8: Days 1 & 11; Cycle 9+: Days 1 & 15); Until subject meets criteria for discontinuation of drug Bortezomib: Solution; IV; 1.3 mg/m²; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of drug. Days of Elotuzumab infusion: Dexamethasone (8mg IV + 8mg Oral) administered. Other days Dexamethasone 20 mg Oral administered Dexamethasone: Tablets; 20 mg; (Cycles 1& 2: once daily on Days 2, 4, 5, 8, 9, 11; Cycles 3-8: once daily on Days 2, 4, 5, 9, 12; Cycles 9+: once daily on Days 2, 8, 9, 16); Until criteria met for discontinuation. Dexamethasone: Tablets; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation of drug. Dexamethasone: Solution; IV; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation

Arm type	Experimental
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	Velcade
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use, Intravenous use

Dosage and administration details:

1.3 mg/m² IV (intravenously) or subcutaneously (SQ)

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid, Solution for injection
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Intravenous and po dexamethasone doses are calculated to provide a total dose that is bioequivalent to the 20 mg oral dose (Dexamethasone 8 mg IV is approximately bioequivalent to 11 mg po).

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

Dosage and administration details:

10 mg/kg IV

Arm title	Bortezomib + Dexamethasone
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Arm description:

Bortezomib: Solution; IV; 1.3 mg/m²; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of study drug. Dexamethasone: Tablets; 20 mg; (Cycles 1-8 once daily on Days 1, 2, 4, 5, 8, 9, 11, 12; Cycles 9+ once daily on Days 1, 2, 8, 9, 15, 16); Until criteria is met for discontinuation of study drug

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid, Solution for injection
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Intravenous and po dexamethasone doses are calculated to provide a total dose that is bioequivalent to the 20 mg oral dose (Dexamethasone 8 mg IV is approximately bioequivalent to 11 mg po).

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	Velcade
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

1.3 mg/m² IV (intravenously) or subcutaneously (SQ)

Number of subjects in period 1^[1]	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone
Started	77	75
Received Treatment	76	74
Completed	0	0
Not completed	77	75
Consent withdrawn by subject	2	5
poor/non-compliance	-	1
Adverse event, non-fatal	2	11
subject request to discontinue treatment	3	5
study drug toxicity	11	14
non-specified	6	4
no longer meets study criteria	1	-
Disease Progression	52	35

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 185 participants were enrolled, 152 participants were randomized. Reasons not randomized: 23 no longer met study criteria, 5 withdrew consent, 2 died, 3 had poor/non-compliance. 150 were treated with study drug. 2 participants were not treated: 1 withdrawal by subject and 1 physician decision.

Baseline characteristics

Reporting groups

Reporting group title	Elotuzumab + Bortezomib + Dexamethasone
Reporting group description:	
Elotuzumab: Solution; Intravenous (IV); 10 mg/kg; (Cycles 1 & 2: Days 1, 8 & 15; Cycles 3-8: Days 1 & 11; Cycle 9+: Days 1 & 15); Until subject meets criteria for discontinuation of drug Bortezomib: Solution; IV; 1.3 mg/m ² ; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of drug. Days of Elotuzumab infusion: Dexamethasone (8mg IV + 8mg Oral) administered. Other days Dexamethasone 20 mg Oral administered Dexamethasone: Tablets; 20 mg; (Cycles 1& 2: once daily on Days 2, 4, 5, 8, 9, 11; Cycles 3-8: once daily on Days 2, 4, 5, 9, 12; Cycles 9+: once daily on Days 2, 8, 9, 16); Until criteria met for discontinuation. Dexamethasone: Tablets; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation of drug. Dexamethasone: Solution; IV; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation	
Reporting group title	Bortezomib + Dexamethasone
Reporting group description:	
Bortezomib: Solution; IV; 1.3 mg/m ² ; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of study drug. Dexamethasone: Tablets; 20 mg; (Cycles 1-8 once daily on Days 1, 2, 4, 5, 8, 9, 11, 12; Cycles 9+ once daily on Days 1, 2, 8, 9, 15, 16); Until criteria is met for discontinuation of study drug	

Reporting group values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone	Total
Number of subjects	77	75	152
Age, Customized			
Less than (<); Greater than, equal to (≥).			
Units: Subjects			
< 65 years	34	33	67
≥65 and <75 years	28	28	56
>= 75 years	15	14	29
Age Continuous			
Units: years			
arithmetic mean	65.4	65.1	
standard deviation	± 9.48	± 10.34	-
Gender, Male/Female			
Units: Subjects			
Female	35	38	73
Male	42	37	79
Region of Enrollment			
Number of subjects enrolled, by country, were summarized.			
Units: Subjects			
United States	25	23	48
Italy	34	32	66
France	10	11	21
Spain	8	9	17
Prior Protease Inhibitor Use			
Categories presented as they were at randomization based on information collected via the Interactive Voice Recognition System (IVRS) system.			
Units: Subjects			
Yes	38	37	75
No	39	38	77

Presence of At Least 1 FcyRIIIa V allele			
An allele is any one of a series of 2 or more different genes that may be on a specific chromosome. Categories presented as they were at randomization based on information collected via the Interactive Voice Recognition System (IVRS) system.			
Units: Subjects			
Yes	55	54	109
No	22	21	43
Number of Prior Lines of Therapy			
Categories presented as they were at randomization based on information collected via the Interactive Voice Recognition System (IVRS) system.			
Units: Subjects			
1 line of prior therapy	55	51	106
2 or 3 lines of prior therapy	22	24	46

End points

End points reporting groups

Reporting group title	Elotuzumab + Bortezomib + Dexamethasone
Reporting group description:	
Elotuzumab: Solution; Intravenous (IV); 10 mg/kg; (Cycles 1 & 2: Days 1, 8 & 15; Cycles 3-8: Days 1 & 11; Cycle 9+: Days 1 & 15); Until subject meets criteria for discontinuation of drug Bortezomib: Solution; IV; 1.3 mg/m ² ; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of drug. Days of Elotuzumab infusion: Dexamethasone (8mg IV + 8mg Oral) administered. Other days Dexamethasone 20 mg Oral administered Dexamethasone: Tablets; 20 mg; (Cycles 1& 2: once daily on Days 2, 4, 5, 8, 9, 11; Cycles 3-8: once daily on Days 2, 4, 5, 9, 12; Cycles 9+: once daily on Days 2, 8, 9, 16); Until criteria met for discontinuation. Dexamethasone: Tablets; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation of drug. Dexamethasone: Solution; IV; 8 mg; (Cycles 1& 2: Days 1, 8, 15; Cycles 3-8: Days 1 & 11; Cycles 9+; Days 1 & 15); Until criteria met for discontinuation	
Reporting group title	Bortezomib + Dexamethasone
Reporting group description:	
Bortezomib: Solution; IV; 1.3 mg/m ² ; (Cycles 1 - 8: Days 1, 4, 8, 11; Cycles 9+: Days 1, 8, 15); Until criteria met for discontinuation of study drug. Dexamethasone: Tablets; 20 mg; (Cycles 1-8 once daily on Days 1, 2, 4, 5, 8, 9, 11, 12; Cycles 9+ once daily on Days 1, 2, 8, 9, 15, 16); Until criteria is met for discontinuation of study drug	

Primary: Median Investigator-Assessed Progression-free survival (PFS) Time (Months) from Randomization to Date of First Tumor Progression or Death due to any Cause - Randomized Participants

End point title	Median Investigator-Assessed Progression-free survival (PFS) Time (Months) from Randomization to Date of First Tumor Progression or Death due to any Cause - Randomized Participants
End point description:	
PE was planned for after at least 103 events; it was analyzed after 111 events. Response was assessed: Day 1 (± 7 days) of each cycle per modified International Myeloma Working Group (IMWG) criteria; assessed using adequate tumor assessment (ATA) (ie, serum and urine M-protein tests performed within 14 days of each other; imaging if baseline measurable extramedullary plasmacytoma existed). Progression: Any of following: Increase of 25% from lowest response in 1 or more: serum and/or urine M-component; in those without measurable serum and urine M-protein levels, difference between involved and uninvolved free light chain (FLC) levels (absolute increase > 100 mg/L); Bone marrow plasma cell percentage (≥10%). Definite new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing lesions or plasmacytomas. Development of hypercalcemia attributed solely to the plasma cell proliferative disorder.	
End point type	Primary
End point timeframe:	
Randomization until 111 events (disease progression or death), up to May 2014, approximately 2 years	

End point values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: Months				
median (confidence interval 95%)	9.7 (7.4 to 12.2)	6.9 (5.1 to 10.2)		

Statistical analyses

Statistical analysis title	Median Progression-free survival
Comparison groups	Elotuzumab + Bortezomib + Dexamethasone v Bortezomib + Dexamethasone
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0923 ^[1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.06

Notes:

[1] - Log Rank test was stratified by prior proteasome inhibitor use (Yes versus No), presence of at least 1 FcyRIIIa V allele (Yes versus No) and number of prior lines of therapy (1 versus 2 or 3) at randomization

Primary: Number of Investigator-Assessed Progression-free survival Events from Randomization to Date of First Tumor Progression or Death Due to Any Cause - All Randomized Participants

End point title	Number of Investigator-Assessed Progression-free survival Events from Randomization to Date of First Tumor Progression or Death Due to Any Cause - All Randomized Participants ^[2]
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End point description:

PE planned for after at least 103 events (progression/death); analyzed at 111 events. Those who neither progressed nor died were censored on the date of last adequate tumor assessment (ATA), which requires both serum and urine M-protein tests. If no post-baseline tumor assessments/no death, then censored on randomization day. Response assessed: Day 1 (\pm 7 days) each cycle; 30 and 60 days post treatment. Modified IMWG criteria used. Progression: Any of following: Increase of 25% in serum and/or urine M-component; if no measurable serum, urine M-protein levels, then difference between involved and uninvolved free light chain (FLC) levels (absolute increase $>$ 100 mg/L) ; Bone marrow plasma cell percentage (\geq 10%). New bone lesions or soft tissue plasmacytomas or increase in size of existing lesions, plasmacytomas. Development of hypercalcemia attributed solely to plasma cell proliferative disorder. First dose occurs within 3 days of randomization.

End point type	Primary
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End point timeframe:

Randomization until 111 events, up to May 2014, approximately 2 years

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint

End point values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: Events (progression or death)	52	59		

Statistical analyses

No statistical analyses for this end point

Primary: 1 Year Progression-Free Survival Rate - Randomized Participants

End point title	1 Year Progression-Free Survival Rate - Randomized Participants ^[3]
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End point description:

PFS rate=Percentage probability of participants experiencing no progression or death up to 1 year, estimated using the Kaplan-Meier method. Response assessed by the investigator: Day 1 (± 7 days) of each cycle per modified IMWG criteria; assessed using ATA (ie, serum and urine M-protein tests performed within 14 days of each other; imaging done if baseline measurable extramedullary plasmacytoma existed). Progression: Any of the following: Increase of 25% from lowest response in 1 or more: serum and/or urine M-component; in those without measurable serum and urine M-protein levels, difference between involved and uninvolved FLC levels (absolute increase > 100 mg/L) ; Bone marrow plasma cell percentage (≥10%). Definite new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing lesions or plasmacytomas. Development of hypercalcemia attributed solely to the plasma cell proliferative disorder.

End point type	Primary
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End point timeframe:

Year 1 after last participant was randomized

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint

End point values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: percentage probability				
number (confidence interval 95%)	0.39 (0.28 to 0.50)	0.33 (0.22 to 0.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-free survival Time (Months) from Randomization to Date of First Tumor Progression or Death due to any cause, in Randomized Participants With at Least One FcyRIIIa V allele

End point title	Median Progression-free survival Time (Months) from
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End point description:

PE was planned for after at least 103 events; it was analyzed after 111 events. Response was assessed: Day 1 (± 7 days) of each cycle per modified IMWG criteria; assessed using adequate tumor assessment (ATA) (ie, serum and urine M-protein tests performed within 14 days of each other; imaging if baseline measurable extramedullary plasmacytoma existed). Progression: Any of following: Increase of 25% from lowest response in 1 or more: serum and/or urine M-component; in those without measurable serum and urine M-protein levels, difference between involved and uninvolved FLC levels (absolute increase > 100 mg/L); Bone marrow plasma cell percentage (≥10%). Definite new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing lesions or plasmacytomas. Development of hypercalcemia attributed solely to the plasma cell proliferative disorder. Randomized participants with at least 1 FcγRIIIa V allele were a sub-set of all randomized participants.

End point type	Secondary
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End point timeframe:

Randomization until 111 events, up to May 2014, approximately 2 years

End point values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: Months				
median (confidence interval 95%)	9.9 (6.1 to 13.9)	8.1 (5.0 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-Assessed Objective Response Rate (ORR) - All Randomized Participants

End point title	Investigator-Assessed Objective Response Rate (ORR) - All Randomized Participants
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End point description:

ORR was calculated for participants with a best overall response (BOR) of partial response (PR) or better, including stringent complete response (sCR), complete response (CR), and very good partial response (VGPR). BOR was determined by the investigator based on myeloma tumor assessments using IMWG criteria: CR=Negative immunofixation of serum and urine and disappearance of any soft tissue plasmacytomas, and < 5% plasma cells in bone marrow; sCR= CR + normal FLC ratio and absence of clonal cells in bone marrow; VGPR=Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein level + urine M-protein level < 100 mg per 24 hour; PR= ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg per 24 hour. ORR= number of participants responding divided by total number of participants randomized, measured as a percentage.

End point type	Secondary
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End point timeframe:

Randomization until 111 events, up to May 2014, approximately 2 years

End point values	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: percentage of participants				
number (confidence interval 95%)	64.9 (53.2 to 75.5)	62.7 (50.7 to 73.6)		

Statistical analyses

Statistical analysis title	Objective Response Rate
Comparison groups	Elotuzumab + Bortezomib + Dexamethasone v Bortezomib + Dexamethasone
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference using Chan-Zhang method
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	17.8

Secondary: Investigator-Assessed Objective Response Rate in Randomized Participants With at Least One FcγRIIIa V Allele

End point title	Investigator-Assessed Objective Response Rate in Randomized Participants With at Least One FcγRIIIa V Allele
End point description:	<p>ORR was calculated for participants with a BOR of PR or better, sCR, CR, and VGPR. BOR was determined by the investigator based on myeloma tumor assessments using IMWG criteria: CR=Negative immunofixation of serum and urine and disappearance of any soft tissue plasmacytomas, and < 5% plasma cells in bone marrow; sCR= CR + normal FLC ratio and absence of clonal cells in bone marrow; VGPR=Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein level + urine M-protein level < 100 mg per 24 hour; PR= ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg per 24 hour. ORR= number of participants responding divided by total number of participants randomized, measured as a percentage. Randomized participants with at least 1 FcγRIIIa V allele were a sub-set of all randomized participants.</p>
End point type	Secondary
End point timeframe:	
Randomization until 111 events, up to May 2014, approximately 2 years	

End point values	Elotuzumab + Bortezomib + Dexamethason e	Bortezomib + Dexamethason e		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: percentage of participants				
number (confidence interval 95%)	60.0 (45.9 to 73.0)	61.1 (46.9 to 74.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Serious Adverse Events were reported from screening period to 60 days from last dose. All Non-Serious Adverse Events were reported from first dose to end of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Elotuzumab + Bortezomib + Dexamethasone
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Reporting group description:

Subjects received treatment of Elotuzumab 10 milligram per kilogram (mg/kg) intravenously (IV) with Bortezomib 1.3 mg/meter square (mg/m²) IV or subcutaneously (SQ). Dexamethasone 20 mg orally in tablet form was given on days when Elotuzumab is not administered, and 8 mg orally in tablet form + 8 mg IV on days when Elotuzumab is administered up to 62 cycles (each cycle is of 21 days for 1-8 cycles and of 28 days for 9-62 cycles).

Reporting group title	Bortezomib + Dexamethasone
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Reporting group description:

Subjects received treatment of Bortezomib 1.3 mg/m² IV or SQ and Dexamethasone 20 mg orally in tablet form to 55 cycles (each cycle is of 21 days for 1-8 cycles and of 28 days for 9-55 cycles).

Serious adverse events	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 75 (52.00%)	31 / 75 (41.33%)	
number of deaths (all causes)	2	6	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	2 / 75 (2.67%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			

subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac chest pain			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oedema peripheral			
subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 75 (1.33%)	3 / 75 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Genital prolapse			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (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			
Acute pulmonary oedema			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Femur fracture			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wrist fracture			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-Respiratory arrest			
subjects affected / exposed	0 / 75 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Coronary artery disease			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	3 / 75 (4.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 75 (2.67%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 75 (5.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	3 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 75 (2.67%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			

subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 75 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 75 (1.33%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 75 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 75 (2.67%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis b			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (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	7 / 75 (9.33%)	5 / 75 (6.67%)	
occurrences causally related to treatment / all	0 / 8	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			

subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 75 (1.33%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	1 / 75 (1.33%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 75 (2.67%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			

subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 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	Elotuzumab + Bortezomib + Dexamethasone	Bortezomib + Dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 75 (96.00%)	71 / 75 (94.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 75 (16.00%)	3 / 75 (4.00%)	
occurrences (all)	24	3	
Hypotension			
subjects affected / exposed	7 / 75 (9.33%)	6 / 75 (8.00%)	
occurrences (all)	7	6	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	20 / 75 (26.67%)	21 / 75 (28.00%)	
occurrences (all)	27	24	
Chest pain			

subjects affected / exposed	6 / 75 (8.00%)	2 / 75 (2.67%)	
occurrences (all)	8	2	
Chills			
subjects affected / exposed	4 / 75 (5.33%)	2 / 75 (2.67%)	
occurrences (all)	6	2	
Face oedema			
subjects affected / exposed	4 / 75 (5.33%)	4 / 75 (5.33%)	
occurrences (all)	4	5	
Influenza like illness			
subjects affected / exposed	7 / 75 (9.33%)	4 / 75 (5.33%)	
occurrences (all)	11	4	
Fatigue			
subjects affected / exposed	22 / 75 (29.33%)	17 / 75 (22.67%)	
occurrences (all)	30	19	
Oedema			
subjects affected / exposed	5 / 75 (6.67%)	3 / 75 (4.00%)	
occurrences (all)	5	3	
Injection site erythema			
subjects affected / exposed	3 / 75 (4.00%)	4 / 75 (5.33%)	
occurrences (all)	3	4	
Oedema peripheral			
subjects affected / exposed	22 / 75 (29.33%)	18 / 75 (24.00%)	
occurrences (all)	26	21	
Pyrexia			
subjects affected / exposed	26 / 75 (34.67%)	15 / 75 (20.00%)	
occurrences (all)	39	22	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	31 / 75 (41.33%)	18 / 75 (24.00%)	
occurrences (all)	44	25	
Dysphonia			
subjects affected / exposed	4 / 75 (5.33%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Dyspnoea			

subjects affected / exposed occurrences (all)	12 / 75 (16.00%) 18	7 / 75 (9.33%) 7	
Epistaxis subjects affected / exposed occurrences (all)	9 / 75 (12.00%) 9	2 / 75 (2.67%) 2	
Productive cough subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 5	5 / 75 (6.67%) 5	
Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 8	7 / 75 (9.33%) 8	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	7 / 75 (9.33%) 8	2 / 75 (2.67%) 2	
Confusional state subjects affected / exposed occurrences (all)	4 / 75 (5.33%) 5	2 / 75 (2.67%) 2	
Depression subjects affected / exposed occurrences (all)	4 / 75 (5.33%) 4	1 / 75 (1.33%) 1	
Insomnia subjects affected / exposed occurrences (all)	20 / 75 (26.67%) 25	15 / 75 (20.00%) 17	
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 6	4 / 75 (5.33%) 4	
Platelet count decreased subjects affected / exposed occurrences (all)	6 / 75 (8.00%) 19	8 / 75 (10.67%) 19	
Weight increased subjects affected / exposed occurrences (all)	4 / 75 (5.33%) 4	4 / 75 (5.33%) 4	
Weight decreased			

subjects affected / exposed occurrences (all)	7 / 75 (9.33%) 7	4 / 75 (5.33%) 4	
Injury, poisoning and procedural complications Rib fracture subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 6	2 / 75 (2.67%) 2	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 3	4 / 75 (5.33%) 5	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	9 / 75 (12.00%) 10	7 / 75 (9.33%) 7	
Dysgeusia subjects affected / exposed occurrences (all)	2 / 75 (2.67%) 2	4 / 75 (5.33%) 4	
Headache subjects affected / exposed occurrences (all)	9 / 75 (12.00%) 9	6 / 75 (8.00%) 6	
Neuralgia subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 6	4 / 75 (5.33%) 4	
Neuropathy peripheral subjects affected / exposed occurrences (all)	28 / 75 (37.33%) 52	28 / 75 (37.33%) 37	
Paraesthesia subjects affected / exposed occurrences (all)	19 / 75 (25.33%) 24	13 / 75 (17.33%) 15	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	8 / 75 (10.67%) 10	9 / 75 (12.00%) 11	
Somnolence subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	6 / 75 (8.00%) 6	
Tremor			

subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 5	5 / 75 (6.67%) 6	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	25 / 75 (33.33%)	20 / 75 (26.67%)	
occurrences (all)	40	26	
Lymphopenia			
subjects affected / exposed	5 / 75 (6.67%)	3 / 75 (4.00%)	
occurrences (all)	16	5	
Thrombocytopenia			
subjects affected / exposed	13 / 75 (17.33%)	22 / 75 (29.33%)	
occurrences (all)	24	41	
Neutropenia			
subjects affected / exposed	4 / 75 (5.33%)	8 / 75 (10.67%)	
occurrences (all)	8	16	
Eye disorders			
Cataract			
subjects affected / exposed	3 / 75 (4.00%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Vision blurred			
subjects affected / exposed	4 / 75 (5.33%)	5 / 75 (6.67%)	
occurrences (all)	4	5	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	9 / 75 (12.00%)	2 / 75 (2.67%)	
occurrences (all)	9	2	
Abdominal pain upper			
subjects affected / exposed	2 / 75 (2.67%)	6 / 75 (8.00%)	
occurrences (all)	2	6	
Abdominal pain			
subjects affected / exposed	8 / 75 (10.67%)	8 / 75 (10.67%)	
occurrences (all)	8	8	
Diarrhoea			
subjects affected / exposed	31 / 75 (41.33%)	24 / 75 (32.00%)	
occurrences (all)	58	39	
Constipation			

subjects affected / exposed	28 / 75 (37.33%)	21 / 75 (28.00%)	
occurrences (all)	33	33	
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 75 (1.33%)	5 / 75 (6.67%)	
occurrences (all)	1	7	
Dyspepsia			
subjects affected / exposed	7 / 75 (9.33%)	5 / 75 (6.67%)	
occurrences (all)	9	5	
Vomiting			
subjects affected / exposed	14 / 75 (18.67%)	7 / 75 (9.33%)	
occurrences (all)	15	7	
Nausea			
subjects affected / exposed	19 / 75 (25.33%)	16 / 75 (21.33%)	
occurrences (all)	28	17	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 75 (2.67%)	5 / 75 (6.67%)	
occurrences (all)	2	6	
Hyperhidrosis			
subjects affected / exposed	4 / 75 (5.33%)	2 / 75 (2.67%)	
occurrences (all)	5	2	
Pruritus			
subjects affected / exposed	4 / 75 (5.33%)	6 / 75 (8.00%)	
occurrences (all)	6	6	
Rash			
subjects affected / exposed	8 / 75 (10.67%)	5 / 75 (6.67%)	
occurrences (all)	14	5	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	4 / 75 (5.33%)	1 / 75 (1.33%)	
occurrences (all)	5	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	14 / 75 (18.67%)	15 / 75 (20.00%)	
occurrences (all)	16	17	
Arthralgia			

subjects affected / exposed	7 / 75 (9.33%)	12 / 75 (16.00%)	
occurrences (all)	9	15	
Bone pain			
subjects affected / exposed	12 / 75 (16.00%)	7 / 75 (9.33%)	
occurrences (all)	16	11	
Muscle spasms			
subjects affected / exposed	5 / 75 (6.67%)	5 / 75 (6.67%)	
occurrences (all)	5	5	
Muscular weakness			
subjects affected / exposed	6 / 75 (8.00%)	2 / 75 (2.67%)	
occurrences (all)	7	2	
Musculoskeletal chest pain			
subjects affected / exposed	7 / 75 (9.33%)	7 / 75 (9.33%)	
occurrences (all)	8	9	
Pain in extremity			
subjects affected / exposed	16 / 75 (21.33%)	12 / 75 (16.00%)	
occurrences (all)	25	15	
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 75 (10.67%)	7 / 75 (9.33%)	
occurrences (all)	11	13	
Conjunctivitis			
subjects affected / exposed	9 / 75 (12.00%)	4 / 75 (5.33%)	
occurrences (all)	12	4	
Herpes zoster			
subjects affected / exposed	6 / 75 (8.00%)	3 / 75 (4.00%)	
occurrences (all)	6	3	
Influenza			
subjects affected / exposed	3 / 75 (4.00%)	7 / 75 (9.33%)	
occurrences (all)	3	7	
Upper respiratory tract infection			
subjects affected / exposed	10 / 75 (13.33%)	4 / 75 (5.33%)	
occurrences (all)	25	4	
Pneumonia			
subjects affected / exposed	1 / 75 (1.33%)	6 / 75 (8.00%)	
occurrences (all)	1	6	

Urinary tract infection subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 3	5 / 75 (6.67%) 9	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 75 (8.00%) 8	4 / 75 (5.33%) 4	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	12 / 75 (16.00%) 16	9 / 75 (12.00%) 9	
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 75 (1.33%) 3	4 / 75 (5.33%) 6	
Hyperglycaemia subjects affected / exposed occurrences (all)	10 / 75 (13.33%) 34	7 / 75 (9.33%) 13	
Hypocalcaemia subjects affected / exposed occurrences (all)	13 / 75 (17.33%) 21	3 / 75 (4.00%) 4	
Hypokalaemia subjects affected / exposed occurrences (all)	8 / 75 (10.67%) 17	5 / 75 (6.67%) 5	
Hyponatraemia subjects affected / exposed occurrences (all)	5 / 75 (6.67%) 5	2 / 75 (2.67%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2012	Broadening the number of lines of prior therapy from 1 - 2 lines to 1 - 3 and allowing up to 15% of subjects to have had prior non-bortezomib proteasome inhibitor therapy. Broadening the stratification criteria to adapt to these changes, ie, stratification of subjects during randomization will be based on subjects have 1 versus 2 or 3 lines of therapy, instead of 1 versus 2 lines of therapy, and subjects being proteasome inhibitor naive versus having had prior proteasome inhibitor exposure, instead of bortezomib naive versus prior bortezomib exposure. Removal of the exclusion criteria describing subjects with uncontrolled diabetes defined as an HbA1c \geq 8.0 and decreasing the disease-free interval for subjects with other prior malignancy from 5 years to 3 years. The dose modification guideline in reference to the adverse event of bortezomib-related peripheral neuropathy is modified to match the bortezomib Prescribing Information. Clarification that once subjects reach cycle 5 without any Grade 2 infusion reactions, the infusion rate at C5D1 should be increased by 1 mL per minute in a stepwise fashion in each cycle up to a maximum of 5 mL per minute.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported