Clinical trial results:
PHASE 2A SINGLE-ARM SAFETY STUDY OF ELOTUZUMAB IN COMBINATION WITH THALIDOMIDE AND DEXAMETHASONE IN SUBJECTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA

Summary

EudraCT number	2011-005121-49
Trial protocol	ES
Global end of trial date	17 March 2016

Results information

Result version number	v1
This version publication date	02 April 2017
First version publication date	02 April 2017

Trial information

Trial identification

Sponsor protocol code	CA204-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01632150
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	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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	17 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of elotuzumab, thalidomide, and dexamethasone (E-Td) in subjects with relapsed and/or refractory multiple myeloma (MM) as assessed by the incidence of severe (Grade 3 or higher) non-hematological adverse events (AEs).

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	24 May 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: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	27
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 51 participants enrolled, 40 received treatment. Of those 40, 11 had cyclophosphamide added to their regimens.

Period 1

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

Arms

Arm title	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide

Arm description:

Participants received thalidomide in 28-day cycles: 50 mg, for the first 2 weeks, escalated to 100 mg for the next 2 weeks and beginning with Cycle 2, to 200 mg once daily. Elotuzumab, 10 mg/kg, was administered as an intravenous infusion weekly for the first 2 cycles and beginning with Cycle 3, every 2 weeks. Dexamethasone, 40 mg, was administered weekly on those weeks when elotuzumab was not administered. On weeks when elotuzumab was also given, participants received dexamethasone as a split dose of 28 mg, 3 to 24 hours before the elotuzumab infusion, and 8 mg intravenously at least 45 minutes before the infusion. Those patients with suboptimal response, defined as evidence of progressive disease between end of Cycle 2 and end of Cycle 4 or inability to achieve partial response or better by end of Cycle 4, also received cyclophosphamide, 50 mg. Cyclophosphamide could not be added beyond Cycle 5.

Arm type	Experimental
Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	BMS-901608, HuLuc63
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Elotuzumab 10 mg/kg was administered as an intravenous (IV) infusion weekly for the first 2 cycles and Q2W beginning with Cycle 3. Treatment was administered in 28-day cycles.

Investigational medicinal product name	Thalidomide
Investigational medicinal product code	
Other name	Thalomid®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Thalidomide was administered by mouth (po) once daily (QD) and escalated from 50 mg for the first 2 weeks to 100 mg for the next 2 weeks and then to 200 mg starting with Cycle 2.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	Decadron®, Dexamethasone Intensol®, Dexpak®, Taperpak®
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Dexamethasone was administered weekly as a 40-mg dose po on weeks without elotuzumab and as a split dose of 28 mg po 3-24 hours before the elotuzumab infusion and 8 mg Intravenously (IV) at least 45 minutes before the start of the infusion on weeks with elotuzumab.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Cytoxan, Endoxan, Neosar
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cyclophosphamide 50 mg po QD was added if the response to E-Td was suboptimal

Number of subjects in period 1[1]	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide
Started	40
Received cyclophosphamide	11
Completed	0
Not completed	40
Consent withdrawn by subject	2
Disease progression	27
Study drug toxicity	1
Unrelated adverse event	7
Patient underwent autologous transplant	1
Moved to compassionate program	2

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: Of 51 participants enrolled, 40 received treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide

Reporting group description:

Participants received thalidomide in 28-day cycles: 50 mg, for the first 2 weeks, escalated to 100 mg for the next 2 weeks and beginning with Cycle 2, to 200 mg once daily. Elotuzumab, 10 mg/kg, was administered as an intravenous infusion weekly for the first 2 cycles and beginning with Cycle 3, every 2 weeks. Dexamethasone, 40 mg, was administered weekly on those weeks when elotuzumab was not administered. On weeks when elotuzumab was also given, participants received dexamethasone as a split dose of 28 mg, 3 to 24 hours before the elotuzumab infusion, and 8 mg intravenously at least 45 minutes before the infusion. Those patients with suboptimal response, defined as evidence of progressive disease between end of Cycle 2 and end of Cycle 4 or inability to achieve partial response or better by end of Cycle 4, also received cyclophosphamide, 50 mg. Cyclophosphamide could not be added beyond Cycle 5.

Reporting group values	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide	Total	
Number of subjects	40	40	
Age Categorical			
Units: Subjects			
Younger than 65 years	22	22	
65 years and older to younger than 75 years	12	12	
75 years and older	6	6	
Age Continuous			
Units: Years			
arithmetic mean	64.3		
standard deviation	± 8.47	-	
Gender, Male/Female			
Units: Subjects			
Female	15	15	
Male	25	25	
Race (NIH/OMB)			
All treated subjects			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	40	40	
More than one race	0	0	
Unknown or Not Reported	0	0	
Myeloma type			
All treated subjects			
Units: Subjects			
Immunoglobulin (Ig)G	15	15	
IGA	7	7	
IGM	0	0	

IGD	0	0	
Light chain disease	9	9	
Not reported	9	9	
Eastern Cooperative Oncology Group (ECOG) performance status			
ECOG is a 6-item scale used to assess disease progression, daily functioning, appropriate treatment, and prognosis. Performance status is scored on a scale ranging from 0-5, with (best score) 0=fully active and able to carry on all predisease performance without restriction and (worst score) 5=death.			
Units: Subjects			
Score 0	17	17	
Score 1	21	21	
Score 2	2	2	

Subject analysis sets

Subject analysis set title	Thalidomide + Elotuzumab + Dexamethasone
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received thalidomide in 28-day cycles: 50 mg, for the first 2 weeks, escalated to 100 mg for the next 2 weeks, then beginning with Cycle 2, to 200 mg once daily. Elotuzumab, 10 mg/kg, was administered as an intravenous infusion weekly for the first 2 cycles, then beginning with Cycle 3, every 2 weeks. Dexamethasone, 40 mg, was administered weekly on those weeks when elotuzumab was not administered. On weeks when elotuzumab was also given, participants received dexamethasone as a split dose of 28 mg, 3 to 24 hours before the elotuzumab infusion, and 8 mg intravenously at least 45 minutes before the infusion.

Reporting group values	Thalidomide + Elotuzumab + Dexamethasone		
Number of subjects	40		
Age Categorical Units: Subjects			
Younger than 65 years	22		
65 years and older to younger than 75 years	12		
75 years and older	6		
Age Continuous Units: Years			
arithmetic mean	64.3		
standard deviation	± 8.47		
Gender, Male/Female Units: Subjects			
Female	15		
Male	25		
Race (NIH/OMB)			
All treated subjects			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	40		
More than one race	0		
Unknown or Not Reported	0		

Myeloma type			
All treated subjects			
Units: Subjects			
Immunoglobulin (Ig)G	15		
IGA	7		
IGM	0		
IGD	0		
Light chain disease	9		
Not reported	9		
Eastern Cooperative Oncology Group (ECOG) performance status			
ECOG is a 6-item scale used to assess disease progression, daily functioning, appropriate treatment, and prognosis. Performance status is scored on a scale ranging from 0-5, with (best score) 0=fully active and able to carry on all predisease performance without restriction and (worst score) 5=death.			
Units: Subjects			
Score 0	17		
Score 1	21		
Score 2	2		

End points

End points reporting groups

Reporting group title	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide

Reporting group description:

Participants received thalidomide in 28-day cycles: 50 mg, for the first 2 weeks, escalated to 100 mg for the next 2 weeks and beginning with Cycle 2, to 200 mg once daily. Elotuzumab, 10 mg/kg, was administered as an intravenous infusion weekly for the first 2 cycles and beginning with Cycle 3, every 2 weeks. Dexamethasone, 40 mg, was administered weekly on those weeks when elotuzumab was not administered. On weeks when elotuzumab was also given, participants received dexamethasone as a split dose of 28 mg, 3 to 24 hours before the elotuzumab infusion, and 8 mg intravenously at least 45 minutes before the infusion. Those patients with suboptimal response, defined as evidence of progressive disease between end of Cycle 2 and end of Cycle 4 or inability to achieve partial response or better by end of Cycle 4, also received cyclophosphamide, 50 mg. Cyclophosphamide could not be added beyond Cycle 5.

Subject analysis set title	Thalidomide + Elotuzumab + Dexamethasone
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received thalidomide in 28-day cycles: 50 mg, for the first 2 weeks, escalated to 100 mg for the next 2 weeks, then beginning with Cycle 2, to 200 mg once daily. Elotuzumab, 10 mg/kg, was administered as an intravenous infusion weekly for the first 2 cycles, then beginning with Cycle 3, every 2 weeks. Dexamethasone, 40 mg, was administered weekly on those weeks when elotuzumab was not administered. On weeks when elotuzumab was also given, participants received dexamethasone as a split dose of 28 mg, 3 to 24 hours before the elotuzumab infusion, and 8 mg intravenously at least 45 minutes before the infusion.

Primary: Percentage of Participants Who Received Treatment Including Cyclophosphamide and Had Grade 3 or Higher Nonhematologic Adverse Events (AEs)

End point title	Percentage of Participants Who Received Treatment Including Cyclophosphamide and Had Grade 3 or Higher Nonhematologic Adverse Events (AEs)[1]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling, Gr 5=Death.

End point type	Primary

End point timeframe:

From the first dose of study drug until the last dose of treatment, including cyclophosphamide treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint.

End point values	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of participants				
number (confidence interval 90%)	62.5 (-99999 to 72.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of All Participants Who Received Treatment Without Cyclophosphamide and Had Grade 3 or Higher Nonhematologic Adverse Events (AEs)

End point title	Percentage of All Participants Who Received Treatment Without Cyclophosphamide and Had Grade 3 or Higher Nonhematologic Adverse Events (AEs)[2]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling, Gr 5=Death.

End point type	Primary

End point timeframe:

From the first dose of study drug until the earlier of discontinuation from E-Td or the time when cyclophosphamide was initiated

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	Thalidomide + Elotuzumab + Dexamethasone			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: Percentage of participants				
number (confidence interval 90%)	55 (-99999 to 65.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Participants Who Received Treatment Including Cyclophosphamide and Had 1 Dose Reduction or Discontinued Due to an Adverse Event

End point title	Percentage of All Participants Who Received Treatment Including Cyclophosphamide and Had 1 Dose Reduction or Discontinued Due to an Adverse Event

End point description:

Elotuzumab dose reduction was not permitted. Thalidomide dose reduction, delay, interruptions, or

discontinuation was permitted in the event of toxicity. Dexamethasone dose reduction was also permitted in the event of toxicity and in the setting of infusion reactions;dose delays were allowed as clinically indicated at the discretion of the investigator. Cyclophosphamide dose reduction, delay, interruption, or discontinuation was permitted in the event of toxicity.

End point type	Secondary

End point timeframe:

From the first dose of study drug until the last dose of treatment, including cyclophosphamide treatment

End point values	Thalidomide + Elotuzumab + Dexamethasone + Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of participants				
number (confidence interval 95%)	65 (48.3 to 79.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Participants Who Received Treatment Without Cyclophosphamide and Had 1 Dose Reduction or Discontinued Due to an Adverse Event

End point title	Percentage of All Participants Who Received Treatment Without Cyclophosphamide and Had 1 Dose Reduction or Discontinued Due to an Adverse Event

End point description:

Elotuzumab dose reduction was not permitted. Thalidomide dose reduction, delay, interruptions, or discontinuation was permitted in the event of toxicity. Dexamethasone dose reduction was also permitted in the event of toxicity and in the setting of infusion reactions;dose delays were allowed as clinically indicated at the discretion of the investigator.

End point type	Secondary

End point timeframe:

From the first dose of study drug until the earlier of discontinuation from E-Td or the time when cyclophosphamide was initiated

End point values	Thalidomide + Elotuzumab + Dexamethasone			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: Percentage of participants				
number (confidence interval 95%)	57.5 (40.9 to 73)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose to 60 days post last dose

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	All Treated Subjects

Reporting group description: -

Serious adverse events	All Treated Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 40 (57.50%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression1			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Plasma cell myeloma			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Cardiac death			

subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Disease progression				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonitis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				

Confusional state			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			
Aspiration bronchial			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocarditis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Herpes zoster			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Aspergillus infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All Treated Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		

Plasma cell myeloma subjects affected / exposed occurrences (all) Plasmacytoma subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2		
Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all)	 4 / 40 (10.00%) 6 4 / 40 (10.00%) 8 2 / 40 (5.00%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Chills	 17 / 40 (42.50%) 25 13 / 40 (32.50%) 21 12 / 40 (30.00%) 12 3 / 40 (7.50%) 3 3 / 40 (7.50%) 3 2 / 40 (5.00%) 2		

subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Crepitations			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Gait disturbance			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	12		
Dyspnoea			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	6		
Catarrh			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Pneumonitis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Productive cough			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Confusional state			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	8		
Weight decreased			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Blood glucose increased			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Laboratory test abnormal			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	11 / 40 (27.50%)		
occurrences (all)	32		
Dizziness			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	9		
Paraesthesia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	11		
Tremor			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	6		
Somnolence			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 40 (37.50%)		
occurrences (all)	26		
Thrombocytopenia			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	14		
Neutropenia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	13		
Eye disorders			

Diplopia subjects affected / exposed occurrences (all) Vision blurred subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 8 / 40 (20.00%) 9 3 / 40 (7.50%) 3 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2		
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 13 / 40 (32.50%) 21		

Bone pain			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	7		
Arthralgia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	12 / 40 (30.00%)		
occurrences (all)	15		
Upper respiratory tract infection			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	10		
Herpes zoster			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	8		
Influenza			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Pneumonia			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Septic shock			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	29		
Decreased appetite			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Iron deficiency			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2013	Subjects who have not started study therapy will be required to have an LVEF of >50%. Additionally, all subjects will undergo an ECG at the start of each 28 day cycle and must have a QTc of < 480 msec in order to receive study drug. Additionally, subjects with more than 4 prior therapies for myeloma will also be excluded.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported