Clinical trial results:
A Multicenter Phase 2 Study of Single-agent Filanesib (ARRY-520) in Patients With Advanced Multiple Myeloma

Summary

EudraCT number	2014-001051-23
Trial protocol	GB DE ES GR BE FR
Global end of trial date	12 September 2017

Results information

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

Trial information

Trial identification

Sponsor protocol code	ARRAY-520-215

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02092922
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Array BioPharma Inc.
Sponsor organisation address	3200 Walnut Street, Boulder, Colorado, United States, 80301
Public contact	Teri Whisenand, Array BioPharma Inc., 001 3033861141, teri.whisenand@arraybiopharma.com
Scientific contact	Teri Whisenand, Array BioPharma Inc., 001 3033861141, teri.whisenand@arraybiopharma.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	05 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2016
Global end of trial reached?	Yes
Global end of trial date	12 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Estimate the objective response rate (ORR) for patients with low Baseline alpha 1-acid glycoprotein (AAG)

Protection of trial subjects:

Approval by the medical ethics committee (EC) and competent authority.
Participation in the study was voluntary and subject to the required patient information and informed consent procedures approved by the EC.
Strict in- and exclusion criteria to assure exclusion of vulnerable participants.
GCP trained staff.

Background therapy:

Filgrastim prophylaxis: Administered as a single daily subcutaneous (SC) bolus injection per the local product prescribing information and institutional guidelines, starting on Day 3 and on Day 17 (each time for a total of 5 to 7 days).
Prophylactic filgrastim allows the administration of higher filanesib doses, providing management of the hematologic effects associated with filanesib exposure and prevention of their complications.

Evidence for comparator:

N/A

Actual start date of recruitment	16 April 2014
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: 13
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	United States: 67
Country: Number of subjects enrolled	Canada: 7
Worldwide total number of subjects	154
EEA total number of subjects	80

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)	69
From 65 to 84 years	85
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Period: 16 April 2014 to 28 July 2015
Territory: Belgium, Canada, France, Germany, Greece, Spain, United Kingdom, United States

Pre-assignment

Screening details:

Screening evaluation included: Obtain written informed consent, record current and past medical history along with all transfusions/plasmaphereses administered, collect histopathologic confirmation of the diagnosis of multiple myeloma, record all prior treatments for multiple myeloma.
A total of 215 subjects were screened

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Filanesib 1.5 mg/m2/day

Arm description:

Filanesib 1.5 mg/m2/day administered IV as a 1-hour (± 10-minute) infusion on Days 1, 2, 15 and 16.

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

Dosage and administration details:

Per 28-day cycle: 1.5 mg/m2/day administered IV as a 1-hour (± 10-minute) infusion on Days 1, 2, 15 and 16.

Number of subjects in period 1	Filanesib 1.5 mg/m2/day
Started	154
Completed	151
Not completed	3
Subjects not treated	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	154	154	
Age categorical			
Age group			
Units: Subjects			
Adults (18-64 years)	69	69	
From 65-84 years	85	85	
85 years and over	0	0	
Gender categorical			
Gender			
Units: Subjects			
Female	63	63	
Male	91	91	

Subject analysis sets

Subject analysis set title	Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat (ITT) Set included all patients who were enrolled for treatment.

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set (SS) included all patients who received 1 or more doses of filanesib.

Subject analysis set title	Response Evaluable Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Response Evaluable Set (RES) included all patients in the SS who had at least 1 post-Baseline disease assessment or who discontinued from the study due to progressive disease (PD), AE or death prior to any disease assessment.
Patients whose disease at Baseline was not measurable or was not refractory to prior cancer treatments per protocol, and patients with other key protocol deviations may have been excluded from this set.

Subject analysis set title	QTc Substudy Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK/QTc Substudy Set included all patients enrolled in the PK/QTc substudy who had at least 1 blood collection for PK with associated bioanalytical results and for whom at least 1 ECG result was obtained.

Reporting group values	Intent-to-treat Set	Safety Set	Response Evaluable Set
Number of subjects	154	151	145
Age categorical			
Age group			
Units: Subjects			

Adults (18-64 years) From 65-84 years 85 years and over	69 85 0		
Gender categorical			
Gender			
Units: Subjects			
Female Male	63 91		

Reporting group values	QTc Substudy Set		
Number of subjects	14		
Age categorical			
Age group			
Units: Subjects			
Adults (18-64 years) From 65-84 years 85 years and over			
Gender categorical			
Gender			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Filanesib 1.5 mg/m2/day
Reporting group description:	
Filanesib 1.5 mg/m2/day administered IV as a 1-hour (± 10-minute) infusion on Days 1, 2, 15 and 16.	
Subject analysis set title	Intent-to-treat Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The intent-to-treat (ITT) Set included all patients who were enrolled for treatment.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set (SS) included all patients who received 1 or more doses of filanesib.	
Subject analysis set title	Response Evaluable Set
Subject analysis set type	Per protocol
Subject analysis set description:	
The Response Evaluable Set (RES) included all patients in the SS who had at least 1 post-Baseline disease assessment or who discontinued from the study due to progressive disease (PD), AE or death prior to any disease assessment. Patients whose disease at Baseline was not measurable or was not refractory to prior cancer treatments per protocol, and patients with other key protocol deviations may have been excluded from this set.	
Subject analysis set title	QTc Substudy Set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The PK/QTc Substudy Set included all patients enrolled in the PK/QTc substudy who had at least 1 blood collection for PK with associated bioanalytical results and for whom at least 1 ECG result was obtained.	

Primary: ORR in patients with low Baseline AAG

End point title	ORR in patients with low Baseline AAG[1]
End point description:	
The ORR was calculated for each AAG subset (Low AAG, High AAG, Unknown AAG) and for all patients in the ITT Set as the proportion of patients whose overall best response by Independent Review (IR) was sCR, CR, very good partial response (VGPR) or partial response (PR). A 95% confidence interval (CI) for each ORR was calculated based on exact binomial distributions.	
End point type	Primary
End point timeframe:	
Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).	

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: No statistical analyses for this end point

End point values	Intent-to-treat Set	Response Evaluable Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	116		
Units: Subjects				
number (not applicable)	9	9		

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in patients with high Baseline AAG

End point title	ORR in patients with high Baseline AAG

End point description:

The ORR was calculated for each AAG subset (Low AAG, High AAG, Unknown AAG) and for all patients in the ITT Set as the proportion of patients whose overall best response by Independent Review (IR) was sCR, CR, very good partial response (VGPR) or partial response (PR). A 95% confidence interval (CI) for each ORR was calculated based on exact binomial distributions.

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set	Response Evaluable Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	25		
Units: Subjects				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Best Response of sCR, CR, VGPR, or PR

End point title	Duration of Best Response of sCR, CR, VGPR, or PR

End point description:

Duration of response is calculated for all patients achieving a sCR, CR, VGPR or PR and is defined as the time from first objective status assessment of sCR/CR/VGPR/PR to the time of first documented disease progression or death. A patient who initiates subsequent myeloma therapy after filanesib discontinuation and before documented disease progression will be censored at the last evaluable disease assessment prior to the start of the subsequent therapy. If a patient has not progressed, died or received subsequent myeloma therapy, the DOR will be censored on the day of the last evaluable disease assessment.

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: months				
median (full range (min-max))	6.7 (1 to 11.5)			

Attachments (see zip file)	Kaplan-Meier Plot Duration of Duration of Best Res/Kaplan-

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Best Response (TBR) of sCR, CR, VGPR, or PR

End point title	Time to Best Response (TBR) of sCR, CR, VGPR, or PR

End point description:

Time to response for patients achieving a sCR, CR, VGPR or PR is defined as the time from first filanesib infusion to the time of first objective status assessment of sCR/CR/VGPR/PR

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: months				
median (full range (min-max))	4.2 (1 to 12.9)			

Attachments (see zip file)	Kaplan-Meier Plot Time to Best Response of sCR, CR/Kaplan-

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Best Response (TBR) of MR

End point title	Time to Best Response (TBR) of MR

End point description:

Time to response for patients achieving an MR is defined as the time from first filanesib infusion to the time of first objective status assessment of MR.

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: months				
median (full range (min-max))	4.4 (1.1 to 9)			

Attachments (see zip file)	Kaplan-Meier Plot Time to Best Response of MR/Kaplan-Meier

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR)

End point title	Clinical Benefit Rate (CBR)

End point description:

Clinical benefit rate is defined as the proportion of patients who achieve ORR or MR (i.e., sCR, CR, VGPR, PR or MR).

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set	Response Evaluable Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154	145		
Units: Subjects				
number (not applicable)	17	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

The disease control rate (DCR) was calculated for each AAG subset and for all patients as the proportion of patients who achieved a best overall response by IR of sCR, CR, VGPR, PR, MR or stable disease (SD) ≥ 8 weeks in duration; 95% CIs calculated for ORR and DCR were based on exact binomial distributions.

End point type	Secondary

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1).

End point values	Intent-to-treat Set	Response Evaluable Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154	145		
Units: Subjects				
number (not applicable)	27	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-free survival is defined as the time from first filanesib infusion to the first documented disease progression or death due to any cause. The date of progression can be the date of PD (for patients not meeting sCR/CR criteria), relapse from sCR/CR if meeting the criteria for progression, or clinical progression. A patient who initiates subsequent myeloma therapy after filanesib discontinuation and before documented disease progression will be censored at the last evaluable disease assessment prior to the start of the subsequent therapy. If a patient has not progressed, died or received subsequent myeloma therapy, the PFS will be censored on the day of the last evaluable disease assessment.
Median PFS and approximate 95% confidence intervals are estimated using Kaplan-Meier PFS techniques.

End point type	Secondary

End point timeframe:

Time from first filanesib infusion to the first documented disease progression or death due to any cause

End point values	Intent-to-treat Set	Intent-to-treat Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154	154		
Units: months				
median (full range (min-max))	2.1 (0 to 15.2)	2.1 (0 to 15.2)		

Attachments (see zip file)	Kaplan-Meier Plot of progression-free survival/Kaplan-Meier

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Treatment (TNT)

End point title	Time to Next Treatment (TNT)

End point description:

Time to next treatment is calculated for all patients and is defined as the time from first filanesib infusion to the time of first subsequent documented myeloma therapy. Patients who have not received subsequent therapy at the time of this analysis (end of study) have been censored at the date of last contact or death due to any cause. Median TNT and approximate 95% confidence intervals are estimated using Kaplan-Meier PFS techniques.

End point type	Secondary

End point timeframe:

Time from first filanesib infusion to the time of first subsequent documented myeloma therapy

End point values	Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	254			
Units: months				
median (full range (min-max))	3.3 (0 to 15.4)			

Attachments (see zip file)	Kaplan-Meier Plot of time to next treatment (TNT)/Kaplan-

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall trial period

Adverse event reporting additional description:

All subjects who were enrolled in the study and received at least one dose of study drug were included in the Safety Set

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Filanesib 1.5 mg/m2/day

Reporting group description:

Filanesib 1.5 mg/m2/day administered IV as a 1-hour (± 10-minute) infusion on Days 1, 2, 15 and 16.

Serious adverse events	Filanesib 1.5 mg/m2/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 151 (28.48%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			

subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Platelet count decreased			
subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urine output decreased			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Wrong drug administered				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	3 / 151 (1.99%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	3 / 151 (1.99%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	1 / 2			
Myocardial ischaemia				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Spinal cord compression				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	6 / 151 (3.97%)			
occurrences causally related to treatment / all	6 / 6			
deaths causally related to treatment / all	0 / 0			
Haematopoietic thrombocytopenia				
subjects affected / exposed	3 / 151 (1.99%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Anaemia				

subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis bullous			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			

subjects affected / exposed	3 / 151 (1.99%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Renal failure			
subjects affected / exposed	1 / 151 (0.66%)		
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	2 / 151 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal pain			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences causally related to treatment / all	3 / 8		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	4 / 151 (2.65%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	1 / 1		

Septic shock			
subjects affected / exposed	2 / 151 (1.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Aspergillus infection			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			

subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningococcal sepsis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic infection				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic colitis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	1 / 151 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyperuricaemia				

subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Filanesib 1.5 mg/m2/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 151 (70.20%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	17 / 151 (11.26%)		
occurrences (all)	17		
Neutrophil count decreased			
subjects affected / exposed	14 / 151 (9.27%)		
occurrences (all)	14		
Platelet count decreased			
subjects affected / exposed	23 / 151 (15.23%)		
occurrences (all)	23		
Weight decreased			
subjects affected / exposed	14 / 151 (9.27%)		
occurrences (all)	14		
White blood cell count decreased			
subjects affected / exposed	12 / 151 (7.95%)		
occurrences (all)	12		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Hypotension			

subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 151 (9.93%)		
occurrences (all)	15		
Dysgeusia			
subjects affected / exposed	8 / 151 (5.30%)		
occurrences (all)	8		
Dizziness			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	43 / 151 (28.48%)		
occurrences (all)	43		
Anaemia			
subjects affected / exposed	72 / 151 (47.68%)		
occurrences (all)	72		
Febrile neutropenia			
subjects affected / exposed	8 / 151 (5.30%)		
occurrences (all)	8		
Neutropenia			
subjects affected / exposed	34 / 151 (22.52%)		
occurrences (all)	34		
Leukopenia			
subjects affected / exposed	11 / 151 (7.28%)		
occurrences (all)	11		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	37 / 151 (24.50%)		
occurrences (all)	37		
Pyrexia			
subjects affected / exposed	23 / 151 (15.23%)		
occurrences (all)	23		
Asthenia			

subjects affected / exposed	17 / 151 (11.26%)		
occurrences (all)	17		
Mucosal inflammation			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	12 / 151 (7.95%)		
occurrences (all)	12		
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	12 / 151 (7.95%)		
occurrences (all)	12		
Nausea			
subjects affected / exposed	33 / 151 (21.85%)		
occurrences (all)	33		
Diarrhoea			
subjects affected / exposed	30 / 151 (19.87%)		
occurrences (all)	30		
Vomiting			
subjects affected / exposed	17 / 151 (11.26%)		
occurrences (all)	17		
Constipation			
subjects affected / exposed	19 / 151 (12.58%)		
occurrences (all)	19		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	17 / 151 (11.26%)		
occurrences (all)	17		
Cough			
subjects affected / exposed	18 / 151 (11.92%)		
occurrences (all)	18		
Epistaxis			
subjects affected / exposed	16 / 151 (10.60%)		
occurrences (all)	16		
Oropharyngeal pain			

subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		
Nasal congestion			
subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	25 / 151 (16.56%)		
occurrences (all)	25		
Bone pain			
subjects affected / exposed	23 / 151 (15.23%)		
occurrences (all)	23		
Pain in extremity			
subjects affected / exposed	15 / 151 (9.93%)		
occurrences (all)	15		
Arthralgia			
subjects affected / exposed	10 / 151 (6.62%)		
occurrences (all)	10		
Musculoskeletal chest pain			
subjects affected / exposed	10 / 151 (6.62%)		
occurrences (all)	10		
Muscle spasms			
subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Musculoskeletal pain			
subjects affected / exposed	9 / 151 (5.96%)		
occurrences (all)	9		
Infections and infestations			
Pneumonia			
subjects affected / exposed	10 / 151 (6.62%)		
occurrences (all)	10		
Respiratory tract infection			

subjects affected / exposed	8 / 151 (5.30%)		
occurrences (all)	8		
Upper respiratory tract infection			
subjects affected / exposed	14 / 151 (9.27%)		
occurrences (all)	14		
Nasopharyngitis			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		
Sinusitis			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	26 / 151 (17.22%)		
occurrences (all)	26		
Hypokalaemia			
subjects affected / exposed	20 / 151 (13.25%)		
occurrences (all)	20		
Hypercalcaemia			
subjects affected / exposed	13 / 151 (8.61%)		
occurrences (all)	13		
Hyperuricaemia			
subjects affected / exposed	12 / 151 (7.95%)		
occurrences (all)	12		
Hyponatraemia			
subjects affected / exposed	8 / 151 (5.30%)		
occurrences (all)	8		
Hypomagnesaemia			
subjects affected / exposed	7 / 151 (4.64%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2015	In order to make the study available to a larger group of appropriate patients, the platelet count required for study entry was reduced to 50 × 10^9/L for all patients, regardless of the % plasma cells in the bone marrow. This change is not expected to result in additional safety concerns, as the dose modification criteria relating to hematologic abnormalities (including thrombocytopenia) have not been changed. Additional substantive changes are as follows: • The upper limit on filanesib dose based on body surface area (BSA) was removed, as it was not supported by safety or pharmacokinetics data to date. • Acceptable methods of skeletal imaging were expanded to include whole-body low-dose computed tomography. • Acceptable methods of plasmacytoma measurement were expanded to include physical examination. • Recommendations regarding dose and duration of prophylactic filgrastim administration were added. • Requirement for a 1-week duration between assessments to confirm PD was removed, as it is not required per IMWG criteria. • Guidance regarding stability of drug product following reconstitution and dilution was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported