Clinical trial results:
Feasibility and Efficacy of dose adjusted Melphalan – Prednisone – Bortezomib (MPV)
in elderly patients 75 years of age with newly diagnosed Multiple Myeloma; a nonrandomised phase II study

Summary

EudraCT number	2013-000320-33
Trial protocol	NL
Global end of trial date	29 June 2022

Results information

Result version number	v1 (current)
This version publication date	06 June 2024
First version publication date	06 June 2024

Trial information

Trial identification

Sponsor protocol code	HOVON_123_MM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON, +31 (0)107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, +31 (0)107041560, hdc@erasmusmc.nl

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	03 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2018
Global end of trial reached?	Yes
Global end of trial date	29 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the feasibility, defined as discontinuation rate, of a dose-adapted MPV scheme in MM patients ≥ 75 years of age

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 240
Worldwide total number of subjects	240
EEA total number of subjects	240

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)	0
From 65 to 84 years	212
85 years and over	28

Subject disposition

Recruitment

Recruitment details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria

Period 1

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

Arms

Arm title	Experimental

Arm description:

Experimental

Arm type	Experimental
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP: Bortezomib
Duration of each cycle is 35 days (every 5 weeks). Total number of cycles is 9.
dose/day: 1.3 mg/m2
Route of administration: s.c.
days of administration: 1, 8, 15, 22

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

Dosage and administration details:

day 1-4 for a maximum of 9 cycles
6 mg/m2 milligram(s)/square meter/day

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

Dosage and administration details:

day 1 to 4 for a maximum of 9 cycles
30 mg/m2 milligram(s)/square meter/ day

Number of subjects in period 1	Experimental
Started	240
Completed	130
Not completed	110
Adverse reactions	39
At patient's request	24
other	15
Lack of efficacy	32

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	240	240	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	212	212	
85 years and over	28	28	
Age continuous Units: years			
median	79		
full range (min-max)	75 to 91	-	
Gender categorical Units: Subjects			
Female	116	116	
Male	124	124	

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description: Experimental	

Primary: primary endpoint

End point title	primary endpoint[1]
End point description:	
End point type	Primary
End point timeframe: see publication	

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: See attached chart/documents for results

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	201			
Units: whole	201			

Attachments (see zip file)	List of reported non-SAE's/nonsaedata123-13Jan2023.pdf Statistical data section from publication/Ho123 publicatie.pdf List of reported SAE's/saedata123-13Jan2023.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs will be reported from the first study-related procedure until 30 days following the last dose of any drug from the protocol treatment schedule or until the start of subsequent systemic therapy for the disease under investigation, if earlier.

Adverse event reporting additional description:

Adverse events occurring after 30 days should also be reported if considered at least possibly related to the investigational medicinal product by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Experimental

Reporting group description: -

Serious adverse events	Experimental		
Total subjects affected by serious adverse events			
subjects affected / exposed	132 / 234 (56.41%)		
number of deaths (all causes)	179		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
AML			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Basal cell carcinoma			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Multiple myeloma progression			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Oesophagus carcinoma			

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal carcinoma				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urotheelcelcarcinoma				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Cerebral ischemia				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Collapse(vasovagal episode)				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intermittent claudication				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				

subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ruptured abdominal aneurysm			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vein thrombosis			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis right leg			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hip surgery			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgery			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Admission pain			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atypical thoracal/precordial pain			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Backpain				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Exacerbation pain				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fever				
subjects affected / exposed	9 / 234 (3.85%)			
occurrences causally related to treatment / all	8 / 14			
deaths causally related to treatment / all	0 / 0			
Fever, unknown cause				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	4 / 234 (1.71%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Non-neutropenic fever				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Overall weakness				

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Recurrent bleeding along catheter vena jugelaris				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death NOS				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Reproductive system and breast disorders				
Ovarian cyst				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Aspiration				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COPD exacerbatie				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnea				

subjects affected / exposed	6 / 234 (2.56%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Exp. COPD				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	4 / 234 (1.71%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Relapse pleural effusion				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Confusion				

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Investigations				
Increased CRP				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Weight loss				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fracture				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Atrial Fibrillation			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cardiac failure			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congestive heart failure			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Decompensatio cordis			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Decompensation cardiac			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Flutter			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Heart failure			
subjects affected / exposed	4 / 234 (1.71%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Mitralis insufficiency			

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NSTEMI				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Right ventricular dysfunction				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
STEMI				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Unstable angina pectoris				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Admission because of dizziness				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 1			
CVA				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ischialgie				

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological paralysis				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Polyneuropathy				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Stroke				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischemic attack				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anemia				
subjects affected / exposed	5 / 234 (2.14%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Anemia / thrombocytopenia				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				

subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenic fever				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	1 / 1			
Thrombopenia				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
(Symtomatic) Anemia				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	4 / 234 (1.71%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Diarrhea				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Emesis				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders other				

subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea and vomiting			
subjects affected / exposed	3 / 234 (1.28%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Rectal bleeding			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting and diarrhea			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Ulcer left foot			
subjects affected / exposed	1 / 234 (0.43%)		
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 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Kidney failure			
subjects affected / exposed	3 / 234 (1.28%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		

Pain right kidney area intermittent				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Progressive renal insufficiency				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal insufficiency				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Backache				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Myopathy				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain back				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain due to MM				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Painfull hip				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Refered pain right leg				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Airway infection				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Catheter related infection				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis of her right leg				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastro				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection leg				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection pulmonary				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection urinarytract				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection without focus				

subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Phlebitis infective			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	26 / 234 (11.11%)		
occurrences causally related to treatment / all	25 / 30		
deaths causally related to treatment / all	1 / 2		
Pneumosepsis			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory infection			
subjects affected / exposed	3 / 234 (1.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	5 / 234 (2.14%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	5 / 234 (2.14%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	3 / 234 (1.28%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Yeast infection				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	4 / 234 (1.71%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Hyper calcemia				
subjects affected / exposed	4 / 234 (1.71%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Hyperglyceamia				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperkalemia				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hyponatremia				

subjects affected / exposed	3 / 234 (1.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Experimental		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	215 / 234 (91.88%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 234 (1.71%)		
occurrences (all)	4		
Vascular disorders			
Vascular disorders			
subjects affected / exposed	17 / 234 (7.26%)		
occurrences (all)	18		
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences (all)	2		
General disorders and administration site conditions			
General disorders and adminstration site conditions	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	90 / 234 (38.46%)		
occurrences (all)	127		
Immune system disorders			
Immune system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 234 (1.28%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 234 (0.43%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	23 / 234 (9.83%)		
occurrences (all)	32		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	14 / 234 (5.98%)		
occurrences (all)	18		
Investigations			
Investigations	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	90 / 234 (38.46%)		
occurrences (all)	294		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 234 (2.14%)		
occurrences (all)	6		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	18 / 234 (7.69%)		
occurrences (all)	19		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	127 / 234 (54.27%)		
occurrences (all)	211		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	52 / 234 (22.22%)		
occurrences (all)	92		
Ear and labyrinth disorders			
Ear and labyrinth disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 234 (0.85%)		
occurrences (all)	2		
Eye disorders			
Eye disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	15 / 234 (6.41%)		
occurrences (all)	18		
Gastrointestinal disorders			

Gastrointestinal disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	86 / 234 (36.75%)		
occurrences (all)	143		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	21 / 234 (8.97%)		
occurrences (all)	23		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	21 / 234 (8.97%)		
occurrences (all)	25		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	45 / 234 (19.23%)		
occurrences (all)	68		
Infections and infestations			
Infections and infestations			
subjects affected / exposed	60 / 234 (25.64%)		
occurrences (all)	76		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	46 / 234 (19.66%)		
occurrences (all)	70		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2015	Expansion of study by 100 patients
26 February 2016	Update to the protocol due to an error in Appendix A

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported