Clinical trial results:
Open-Label, Single-Arm Study of the Safety and Efficacy of CC-5013 Monotherapy for Subjects with Multiple Myeloma: a Companion Study for Studies Thal-MM-003, CC-5013-MM-009, and CC-5013-MM-010.

Summary

EudraCT number	2004-002102-30
Trial protocol	IT
Global end of trial date	11 November 2013

Results information

Result version number	v1 (current)
This version publication date	25 April 2022
First version publication date	25 April 2022

Trial information

Trial identification

Sponsor protocol code	CC-5013-MM-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00622336
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of CC-5013 monotherapy in patients with advanced multiple myeloma who discontinued treatment with combination thalidomide plus high-dose dexamethasone or high-dose dexamethasone alone in studies Thal-MM-003, CC-5013-MM-009 and CC-5013-MM-010 due to the development of documented disease progression or the inability to tolerate the lowest dosing regimen per previous protocol of thalidomide and/or high-dose dexamethasone without Grade 3 or 4 toxicity.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2003
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 119
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Ukraine: 43
Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	Australia: 37
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Spain: 27
Worldwide total number of subjects	330
EEA total number of subjects	55

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)	194
From 65 to 84 years	135
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

330 subjects were treated.

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lenalidomide 25mg

Arm description:

Lenalidomide 25mg by mouth (PO) daily on Days 1 to 21 in each 28 day cycle

Arm type	Experimental
Investigational medicinal product name	CC-5013
Investigational medicinal product code	
Other name	Revlimid
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide 25mg capsules daily on Days 1 to 21 in each 28 day treatment cycle

Number of subjects in period 1	Lenalidomide 25mg
Started	330
Completed	21
Not completed	309
Adverse event, serious fatal	14
Consent withdrawn by subject	13
Progression of Disease	181
Adverse event, non-fatal	46
Lack of therapeutic effect	13
Other reasons	40
Lost to follow-up	2

Period 2	
Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Arm title	Lenalidomide 25mg

Arm description:

Lenalidomide 25mg by mouth (PO) daily on Days 1 to 21 in each 28 day cycle

Arm type	Experimental
Investigational medicinal product name	CC-5013
Investigational medicinal product code	
Other name	Revlimid
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide 25mg capsules daily on Days 1 to 21 in each 28 day treatment cycle

Number of subjects in period 2	Lenalidomide 25mg
Started	21
Completed	0
Not completed	21
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Progressive Disease	6
Lack of therapeutic effect	2
Other reasons	9
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Lenalidomide 25mg
Reporting group description: Lenalidomide 25mg by mouth (PO) daily on Days 1 to 21 in each 28 day cycle	

Reporting group values	Lenalidomide 25mg	Total	
Number of subjects	330	330	
Age, Customized Units: Subjects			
> 65 years|	136	136	
≤ 65 years|	194	194	
Age Continuous Units: years			
arithmetic mean	63.3		
standard deviation	± 9.43	-	
Gender, Male/Female Units: Subjects			
Female	137	137	
Male	193	193	
Race/Ethnicity, Customized Units: Subjects			
Asian/Pacific Islander|	2	2	
Black or African American|	14	14	
White|	309	309	
Hispanic|	5	5	

End points

End points reporting groups

Reporting group title	Lenalidomide 25mg
Reporting group description: Lenalidomide 25mg by mouth (PO) daily on Days 1 to 21 in each 28 day cycle	
Reporting group title	Lenalidomide 25mg
Reporting group description: Lenalidomide 25mg by mouth (PO) daily on Days 1 to 21 in each 28 day cycle	

Primary: Number of Participants with Adverse Events (AE) During the Treatment Phase

End point title	Number of Participants with Adverse Events (AE) During the Treatment Phase[1]

End point description:

An AE is any sign, symptom, illness, or diagnosis (either observed or volunteered) that appears or worsens during the course of the study Serious adverse event (SAE) = any AE which results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect; constitutes an important medical event. A treatment emergent AE is defined as any AE occurring or worsening on or after the first dose of study drug and within 30 days after the last dose of study drug. Safety and severity was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 2.0; Severity of AEs were graded (including second primary malignancies) as Grade 1- Mild; Grade 2- Moderate; Grade 3- Severe; Grade 4- Life-threatening; Grade 5-Fatal;

End point type	Primary

End point timeframe:

Until data cut-off date of of 22 Oct 2009; AEs/SAEs were recorded from informed consent to 30 days post treatment discontinuation visit; maximum exposure days on study drug was 1260 days

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 were performed for this endpoint

End point values	Lenalidomide 25mg			
Subject group type	Reporting group			
Number of subjects analysed	330			
Units: participants				
Adverse Event (AE)	327			
Adverse Event Related to Study Drug	268			
Grade 3 or 4 Adverse Event	256			
Serious Adverse Event (SAE)	177			
AEs Leading to Discontinuation of study drug	52			
AEs leading to Dose Reduction/Interruption	210			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AE) During the Extension Phase

End point title	Number of Participants with Adverse Events (AE) During the Extension Phase[2]

End point description:

An AE is any sign, symptom, illness, or diagnosis (either observed or volunteered) that appears or worsens during the course of the study Serious adverse event (SAE) = any AE which results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect; constitutes an important medical event. A treatment emergent AE is defined as any AE occurring or worsening on or after the first dose of study drug and within 30 days after the last dose of study drug. Safety and severity was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 2.0; Severity of AEs were graded (including second primary malignancies) as Grade 1- Mild; Grade 2- Moderate; Grade 3- Severe; Grade 4- Life-threatening; Grade 5-Fatal;

End point type	Primary

End point timeframe:

From 22 October 2009 to November 2013; AEs/Serious AEs were recorded from informed consent to 30 days post treatment discontinuation visit.

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: No statistical analyses were performed for this endpoint

End point values	Lenalidomide 25mg			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
Adverse Event (AE)	13			
Adverse Event related to study drug	1			
Grade 3 or 4 Adverse Event	5			
Serious Adverse Event (SAE)	5			
AEs leading to discontinuation of study drug	1			
AEs leading to dose reduction/interruption	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of response based on the Myeloma response determination criteria developed by Bladé et al 1998 and defined as time from the initial documented response (partial response or better) to confirmed disease progression, based on International Myeloma Working Group (IMWG) criteria.

End point type	Secondary

End point timeframe:

Up to 70 months

End point values	Lenalidomide 25mg			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Months				
median (full range (min-max))	(to)			

Notes:

[3] - Duration of response not analyzed per the sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Myeloma Response Rate

End point title	Myeloma Response Rate

End point description:

Myeloma response determination criteria developed by Bladé et al 1998. Complete Response (CR):Disappearance of monoclonal paraprotein. Remission Response (RR):75-99% reduction in monoclonal paraprotein/90-99% reduction in 24-hr urinary light chain excretion. Partial Response (PR):50-74% reduction in monoclonal paraprotein/50-89% reduction in 24-hr urinary light chain excretion. Stable Disease (SD):Criteria for PR or PD not met. Plateau Phase:If PR, stable monoclonal paraprotein (within 25% above or below nadir)/stable soft tissue plasmacytomas. Progressive Disease (PD):Disease worsens.

End point type	Secondary

End point timeframe:

Up to 70 months

End point values	Lenalidomide 25mg			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Percentage of participants				
number (not applicable)				

Notes:

[4] - Myeloma Response Rate not analyzed per the sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

End point title	Time to Progression

End point description:

Time to progression based on the myeloma response determination criteria developed by Bladé et al 1998 and is defined as the time from registration to the first documented progression. The progressive disease criteria included increasing monoclonal paraprotein levels, bone marrow findings, worsening lytic bone disease, progressively enlarging extramedullary plasmacytomas, or hypercalcemia.

End point type	Secondary

End point timeframe:

Up to 70 months

End point values	Lenalidomide 25mg			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Months				
number (not applicable)				

Notes:

[5] - Time to progression not analyzed per the sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through to 30 days after the last dose.

Adverse event reporting additional description:

Data is reported in 2 groups:
1) Events occurred within the data cutoff of 22 Oct 2009 (for all the subjects, regardless of whether they continued to the Extension Phase)
2) Events occurred from 22 Oct 2009 to 11 Nov 2013 (only for those subjects who continued in the Extension phase)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	5.1

Reporting groups

Reporting group title	Extension Phase (from 22 Oct 2009 to 11 Nov 2013)

Reporting group description:

Lenalidomide 25mg by mouth daily on Days 1 to 21 in each 28 day cycle

Reporting group title	Treatment Phase (up to 22 Oct 2009)

Reporting group description:

Lenalidomide 25mg by mouth daily on Days 1 to 21 in each 28 day cycle

Serious adverse events	Extension Phase (from 22 Oct 2009 to 11 Nov 2013)	Treatment Phase (up to 22 Oct 2009)	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 21 (23.81%)	177 / 330 (53.64%)	
number of deaths (all causes)	1	28	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer NOS			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniopharyngioma			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Light chain disease			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer stage unspecified (excl metastatic tumours to lung)			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesothelioma			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple myeloma			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			

subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)	7 / 330 (2.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 21 (4.76%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site cellulitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	14 / 330 (4.24%)	
occurrences causally related to treatment / all	0 / 0	4 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis NOS			
subjects affected / exposed	1 / 21 (4.76%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive airways disease			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)	5 / 330 (1.52%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary thrombosis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 21 (0.00%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function tests NOS abnormal			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial injury NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirenal haematoma			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure NOS			
subjects affected / exposed	1 / 21 (4.76%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema NOS			
subjects affected / exposed	0 / 21 (0.00%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sick sinus syndrome			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phantom pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculitis brachial			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia of malignant disease			
subjects affected / exposed	1 / 21 (4.76%)	0 / 330 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia NOS			

subjects affected / exposed	1 / 21 (4.76%)	11 / 330 (3.33%)	
occurrences causally related to treatment / all	0 / 1	7 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	9 / 330 (2.73%)	
occurrences causally related to treatment / all	0 / 0	10 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperviscosity syndrome			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia NOS			
subjects affected / exposed	0 / 21 (0.00%)	5 / 330 (1.52%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	9 / 330 (2.73%)	
occurrences causally related to treatment / all	0 / 0	6 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain NOS			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea NOS			
subjects affected / exposed	1 / 21 (4.76%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis NOS			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage NOS			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal pain NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia NOS			
subjects affected / exposed	1 / 21 (4.76%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periproctitis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute NOS			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis medicamentosa			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Azotaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure NOS			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute on chronic			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	1 / 21 (4.76%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 21 (0.00%)	8 / 330 (2.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw osteitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised osteoarthritis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis NOS			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in limb			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective NOS			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 21 (0.00%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis acute NOS			
subjects affected / exposed	0 / 21 (0.00%)	3 / 330 (0.91%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus sepsis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia NOS			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive chronic bronchitis with acute exacerbation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia NOS			
subjects affected / exposed	2 / 21 (9.52%)	38 / 330 (11.52%)	
occurrences causally related to treatment / all	0 / 2	8 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis NOS			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	6 / 330 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection NOS			
subjects affected / exposed	1 / 21 (4.76%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus NOS			
subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 21 (0.00%)	4 / 330 (1.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperproteinaemia			

subjects affected / exposed	0 / 21 (0.00%)	2 / 330 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Extension Phase (from 22 Oct 2009 to 11 Nov 2013)	Treatment Phase (up to 22 Oct 2009)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 21 (28.57%)	307 / 330 (93.03%)	
Vascular disorders			
Hypertension NOS			
subjects affected / exposed	0 / 21 (0.00%)	25 / 330 (7.58%)	
occurrences (all)	0	28	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 21 (14.29%)	61 / 330 (18.48%)	
occurrences (all)	3	89	
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	17 / 330 (5.15%)	
occurrences (all)	0	20	
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	94 / 330 (28.48%)	
occurrences (all)	0	130	
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)	49 / 330 (14.85%)	
occurrences (all)	0	65	
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	59 / 330 (17.88%)	
occurrences (all)	0	83	
Pain NOS			

subjects affected / exposed	0 / 21 (0.00%)	25 / 330 (7.58%)	
occurrences (all)	0	33	
Respiratory, thoracic and mediastinal disorders			
Bronchitis NOS			
subjects affected / exposed	0 / 21 (0.00%)	26 / 330 (7.88%)	
occurrences (all)	0	36	
Cough			
subjects affected / exposed	0 / 21 (0.00%)	63 / 330 (19.09%)	
occurrences (all)	0	94	
Dyspnoea NOS			
subjects affected / exposed	0 / 21 (0.00%)	44 / 330 (13.33%)	
occurrences (all)	0	55	
Nasopharyngitis			
subjects affected / exposed	0 / 21 (0.00%)	46 / 330 (13.94%)	
occurrences (all)	0	95	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 21 (0.00%)	20 / 330 (6.06%)	
occurrences (all)	0	27	
Depression			
subjects affected / exposed	0 / 21 (0.00%)	20 / 330 (6.06%)	
occurrences (all)	0	20	
Insomnia			
subjects affected / exposed	0 / 21 (0.00%)	39 / 330 (11.82%)	
occurrences (all)	0	53	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	35 / 330 (10.61%)	
occurrences (all)	0	41	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 21 (0.00%)	24 / 330 (7.27%)	
occurrences (all)	0	29	
Headache			
subjects affected / exposed	3 / 21 (14.29%)	45 / 330 (13.64%)	
occurrences (all)	3	82	

Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	40 / 330 (12.12%)	
occurrences (all)	0	57	
Peripheral neuropathy NOS			
subjects affected / exposed	0 / 21 (0.00%)	25 / 330 (7.58%)	
occurrences (all)	0	34	
Blood and lymphatic system disorders			
Leukopenia NOS			
subjects affected / exposed	0 / 21 (0.00%)	22 / 330 (6.67%)	
occurrences (all)	0	48	
Anaemia NOS			
subjects affected / exposed	2 / 21 (9.52%)	117 / 330 (35.45%)	
occurrences (all)	3	189	
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	158 / 330 (47.88%)	
occurrences (all)	0	492	
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	65 / 330 (19.70%)	
occurrences (all)	0	115	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 21 (0.00%)	23 / 330 (6.97%)	
occurrences (all)	0	28	
Gastrointestinal disorders			
Abdominal pain NOS			
subjects affected / exposed	0 / 21 (0.00%)	25 / 330 (7.58%)	
occurrences (all)	0	30	
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	86 / 330 (26.06%)	
occurrences (all)	0	105	
Diarrhoea NOS			
subjects affected / exposed	0 / 21 (0.00%)	92 / 330 (27.88%)	
occurrences (all)	0	140	
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	20 / 330 (6.06%)	
occurrences (all)	0	29	
Vomiting NOS			

subjects affected / exposed	0 / 21 (0.00%)	33 / 330 (10.00%)	
occurrences (all)	0	41	
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	73 / 330 (22.12%)	
occurrences (all)	0	110	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 21 (0.00%)	30 / 330 (9.09%)	
occurrences (all)	0	32	
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	48 / 330 (14.55%)	
occurrences (all)	0	64	
Rash NOS			
subjects affected / exposed	0 / 21 (0.00%)	60 / 330 (18.18%)	
occurrences (all)	0	98	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	72 / 330 (21.82%)	
occurrences (all)	0	107	
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	76 / 330 (23.03%)	
occurrences (all)	0	114	
Bone pain			
subjects affected / exposed	0 / 21 (0.00%)	58 / 330 (17.58%)	
occurrences (all)	0	87	
Chest wall pain			
subjects affected / exposed	0 / 21 (0.00%)	24 / 330 (7.27%)	
occurrences (all)	0	31	
Muscle cramp			
subjects affected / exposed	0 / 21 (0.00%)	54 / 330 (16.36%)	
occurrences (all)	0	94	
Pain in limb			
subjects affected / exposed	0 / 21 (0.00%)	45 / 330 (13.64%)	
occurrences (all)	0	62	
Infections and infestations			

Upper respiratory tract infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	67 / 330 (20.30%)	
occurrences (all)	0	145	
Urinary tract infection NOS			
subjects affected / exposed	0 / 21 (0.00%)	17 / 330 (5.15%)	
occurrences (all)	0	38	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 21 (0.00%)	41 / 330 (12.42%)	
occurrences (all)	0	46	
Appetite decreased NOS			
subjects affected / exposed	0 / 21 (0.00%)	22 / 330 (6.67%)	
occurrences (all)	0	28	
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)	21 / 330 (6.36%)	
occurrences (all)	0	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2003	1. The schedule of laboratory procedures was streamlined. 2. Protein electrophoresis and quantitative immunoglobulins were rescheduled to baseline, treatment discontinuation, and only if clinically indicated at all other visits. 3. Bone marrow aspiration/biopsy was rescheduled to baseline and only if clinically indicated thereafter. 4. Skeletal survey was rescheduled to baseline and to confirm complete response at discontinuation from treatment; thereafter, performed only if clinically indicated. 5. Immunofixation was rescheduled to baseline and only to confirm complete response thereafter.
09 June 2006	1. Clarified exclusionary hematology laboratory criteria. 2. Modified pregnancy language as stipulated in the RevAssist® program.
14 August 2006	1. Serum Beta-2 microglobulin added to Schedule of Study Assessments (screening). 2. Statement that "lenalidomide in combination with dexamethasone was also approved for the treatment of patients with multiple myeloma who have received at least one prior therapy" was added to the introduction.
16 June 2009	1. Enrollment into the study was terminated. 2. Subjects currently enrolled and receiving lenalidomide were given the opportunity to continue to receive lenalidomide from Celgene in the US and in other countries where this is possible without cost to the subject. 3. Subjects currently enrolled in Poland, Russia, and the Ukraine were given the opportunity to continue to receive lenalidomide via an extension phase and be monitored for safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported