Clinical trial results:
An Open-Label, Dose-Escalation, Phase 1/2 Study of the Oral Form of Ixazomib (MLN9708), a Next-Generation Proteasome Inhibitor, Administered in Combination with a Standard Care Regimen of Melphalan and Prednisone in Patients with Newly Diagnosed Multiple Myeloma Requiring Systemic Treatment

Summary

EudraCT number	2010-023772-71
Trial protocol	ES CZ GB IT
Global end of trial date	29 December 2016

Results information

Result version number	v1 (current)
This version publication date	18 January 2018
First version publication date	18 January 2018

Trial information

Trial identification

Sponsor protocol code	C16006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01335685
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	Millennium Pharmaceuticals, Inc., 40 Landsdowne Street, United States,
Public contact	Medical Director, Takeda, +1 8778253327, trialdisclosures@takeda.com
Scientific contact	Medical Director, Takeda, +1 8778253327, trialdisclosures@takeda.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	29 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2016
Global end of trial reached?	Yes
Global end of trial date	29 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to determine the safety, maximum tolerated dose (MTD), and recommended phase 2 dose (RP2D) of oral ixazomib.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Czech Republic: 15
Worldwide total number of subjects	61
EEA total number of subjects	49

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)	1
From 65 to 84 years	59
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 14 investigative sites in United States, Canada, United Kingdom, Spain and Czech Republic from 27 June 2011 to 29 December 2016.

Pre-assignment

Screening details:

Participants with a diagnosis of multiple myeloma were enrolled to receive ixazomib orally at various doses in Phase 1. Only Arm B: Ixazomib 4.0 mg continued in Phase 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Ixazomib 3.0 mg

Arm description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle for up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 23 maintenance cycles; overall up to 32 cycles [34 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 3.0 mg, capsule, on Days 1, 4, 8, 11, 22, 25, 29, 32 in 42-day cycle up to 9 cycles

Arm title	Arm A: Ixazomib 3.7 mg

Arm description:

Ixazomib 3.7 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 10 maintenance cycles; overall up to 19 cycles [21 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 3.7 mg, capsules, on Days 1, 4, 8, 11, 22, 25, 29, 32 in 42-day cycle up to 9 cycles

Arm title	Arm B: Ixazomib 3.0 mg

Arm description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally on Days 1

to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 15 maintenance cycles; overall up to 27 cycles [25 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 3.0 mg, capsules, on Days 1, 8, 15 up to 13 cycles in 28-day cycle

Arm title	Arm B: Ixazomib 4.0 mg

Arm description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 cycle plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles [58 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 up to 13 cycles in 28-day cycle

Arm title	Arm B: Ixazomib 5.5 mg

Arm description:

Ixazomib 5.5 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 24 cycles [24 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 5.5 mg, capsules, on Days 1, 8, 15 up to 13 cycles in 28-day cycle

Arm title	Arm C: Ixazomib 3.0 mg

Arm description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 30 maintenance cycles; overall up to 39 cycles [40 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 3.0 mg, capsules, on Days 1, 8, 15, 22, and 29 up to 9 cycles in 42-day cycle

Arm title	Arm C: Ixazomib 4.0 mg

Arm description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 21 cycles [24 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 4.0 mg, capsules, on Days 1, 8, 15, 22, and 29 up to 9 cycles in 42-day cycle

Arm title	Arm D: Ixazomib 4.0 mg

Arm description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 28 maintenance cycles; overall up to 37 cycles [38 months]).

Arm type	Experimental
Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib 4.0 mg, capsules, on Days 1, 8, 22, and 29 in 42-day cycle up to 13 cycles

Number of subjects in period 1	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg
Started	7	4	3
Completed	4	3	1
Not completed	3	1	2
Consent withdrawn by subject	1	-	-
Study Terminated by Sponsor	2	1	1
Reason not Specified	-	-	1

Consent withdrawn by subject	1	-	-
Study Terminated by Sponsor	10	-	4
Reason not Specified	-	-	1

Number of subjects in period 1	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Started	4	6
Completed	2	3
Not completed	2	3
Consent withdrawn by subject	-	-
Study Terminated by Sponsor	2	3
Reason not Specified	-	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle for up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 23 maintenance cycles; overall up to 32 cycles [34 months]).

Reporting group title	Arm A: Ixazomib 3.7 mg

Reporting group description:

Ixazomib 3.7 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 10 maintenance cycles; overall up to 19 cycles [21 months]).

Reporting group title	Arm B: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 15 maintenance cycles; overall up to 27 cycles [25 months]).

Reporting group title	Arm B: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 cycle plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles [58 months]).

Reporting group title	Arm B: Ixazomib 5.5 mg

Reporting group description:

Ixazomib 5.5 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 24 cycles [24 months]).

Reporting group title	Arm C: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 30 maintenance cycles; overall up to 39 cycles [40 months]).

Reporting group title	Arm C: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 21 cycles [24 months]).

Reporting group title	Arm D: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving

benefit in maintenance phase (up to 28 maintenance cycles; overall up to 37 cycles [38 months]).

Reporting group values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg
Number of subjects	7	4	3
Age, Customized Units: Subjects			
<75|	6	0	2
>=75|	1	4	1
Age Continuous Units: years			
arithmetic mean	71.0	79.8	73.0
standard deviation	± 6.14	± 2.87	± 7.55
Gender, Male/Female Units: Subjects			
Female	5	3	1
Male	2	1	2
Race/Ethnicity, Customized Units: Subjects			
Missing|	1	1	1
Not Hispanic or Latino|	6	3	2
Race/Ethnicity, Customized Units: Subjects			
Asian|	0	0	0
Black or African American|	0	0	0
White|	6	4	3
Other|	1	0	0
Height Units: cm			
arithmetic mean	163.37	160.25	160.10
standard deviation	± 8.023	± 8.342	± 13.286
Weight at Baseline Units: kg			
arithmetic mean	69.41	72.63	78.97
standard deviation	± 6.703	± 13.972	± 18.224
Body Surface Area at Baseline			
Body Surface Area (m^2) = square root [height (cm) x weight (kg) / 3600].			
Units: m^2			
arithmetic mean	1.773	1.798	1.870
standard deviation	± 0.1027	± 0.2148	± 0.2740

Reporting group values	Arm B: Ixazomib 4.0 mg	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg
Number of subjects	26	5	6
Age, Customized Units: Subjects			
<75|	15	2	1
>=75|	11	3	5

Age Continuous Units: years			
arithmetic mean	74.5	74.2	75.8
standard deviation	± 4.52	± 5.63	± 4.96
Gender, Male/Female Units: Subjects			
Female	16	5	4
Male	10	0	2
Race/Ethnicity, Customized Units: Subjects			
Missing|	2	0	0
Not Hispanic or Latino|	24	5	6
Race/Ethnicity, Customized Units: Subjects			
Asian|	0	0	1
Black or African American|	1	0	0
White|	24	5	5
Other|	1	0	0
Height Units: cm			
arithmetic mean	164.02	157.52	161.70
standard deviation	± 12.869	± 6.103	± 15.361
Weight at Baseline Units: kg			
arithmetic mean	75.23	60.76	70.67
standard deviation	± 17.037	± 7.747	± 25.616
Body Surface Area at Baseline			
Body Surface Area (m^2) = square root [height (cm) x weight (kg) / 3600].			
Units: m^2			
arithmetic mean	1.843	1.630	1.734
standard deviation	± 0.2749	± 0.1275	± 0.4380

Reporting group values	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg	Total
Number of subjects	4	6	61
Age, Customized Units: Subjects			
<75|	1	4	31
>=75|	3	2	30
Age Continuous Units: years			
arithmetic mean	77.0	73.2	
standard deviation	± 3.56	± 9.66	-
Gender, Male/Female Units: Subjects			
Female	1	3	38
Male	3	3	23
Race/Ethnicity, Customized Units: Subjects			
Missing|	0	0	5
Not Hispanic or Latino|	4	6	56
Race/Ethnicity, Customized			

Units: Subjects			
Asian|	0	0	1
Black or African American|	0	0	1
White|	4	6	57
Other|	0	0	2
Height			
Units: cm			
arithmetic mean	168.00	164.50	
standard deviation	± 1.826	± 11.413	-
Weight at Baseline			
Units: kg			
arithmetic mean	75.93	66.97	
standard deviation	± 12.207	± 21.404	-
Body Surface Area at Baseline			
Body Surface Area (m^2) = square root [height (cm) x weight (kg) / 3600].			
Units: m^2			
arithmetic mean	1.880	1.718	
standard deviation	± 0.1592	± 0.3650	-

End points

End points reporting groups

Reporting group title	Arm A: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle for up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 23 maintenance cycles; overall up to 32 cycles [34 months]).

Reporting group title	Arm A: Ixazomib 3.7 mg

Reporting group description:

Ixazomib 3.7 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 10 maintenance cycles; overall up to 19 cycles [21 months]).

Reporting group title	Arm B: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 15 maintenance cycles; overall up to 27 cycles [25 months]).

Reporting group title	Arm B: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 cycle plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles [58 months]).

Reporting group title	Arm B: Ixazomib 5.5 mg

Reporting group description:

Ixazomib 5.5 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 24 cycles [24 months]).

Reporting group title	Arm C: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 30 maintenance cycles; overall up to 39 cycles [40 months]).

Reporting group title	Arm C: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 21 cycles [24 months]).

Reporting group title	Arm D: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving

benefit in maintenance phase (up to 28 maintenance cycles; overall up to 37 cycles [38 months]).

Subject analysis set title	Arm A: Ixazomib 3.0 - 3.7 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ixazomib 3.0 - 3.7 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally, on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 23 maintenance cycles; overall up to 32 cycles).

Subject analysis set title	Arm B: Ixazomib 3.0 - 5.5 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ixazomib 3.0 - 5.5 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally, on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1-4 for in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles).

Subject analysis set title	Arm C: Ixazomib 3.0 - 4.0 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ixazomib 3.0 - 4.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally, on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 30 maintenance cycles; overall up to 39 cycles).

Subject analysis set title	Arm D: Ixazomib 4.0 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles in maintenance phase (up to 28 maintenance cycles; overall up to 37 cycles).

Subject analysis set title	Arm B: Ixazomib 4.0 mg (RP2D)
Subject analysis set type	Full analysis

Subject analysis set description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally, on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles [58 months]).

Primary: Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Ixazomib (Phase 1)

End point title	Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Ixazomib (Phase 1)[1]

End point description:

The RP2D is the maximum tolerated dose (MTD) or less. The MTD is defined as the dose range at which ≤ 1 of 6 evaluable participants experience dose limiting toxicities (DLT) within the first 28 days of treatment (end of cycle 1).

End point type	Primary

End point timeframe:

Cycle 1, phase 1 (Up to 42 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: Statistical analysis was not reported as only descriptive analysis was performed as planned.

End point values	Arm A: Ixazomib 3.0 - 3.7 mg	Arm B: Ixazomib 3.0 - 5.5 mg	Arm C: Ixazomib 3.0 - 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	34	10	6
Units: mg				
number (not applicable)	3	4	3	4

Statistical analyses

No statistical analyses for this end point

Primary: Very Good Partial Response (VGPR) or Better Response Rate (Phase 2)

End point title	Very Good Partial Response (VGPR) or Better Response Rate (Phase 2)[2]

End point description:

VGPR or better response rate is defined as percentage of participants with a complete response (CR) and very good partial response (VGPR). Per International Myeloma Working Group Uniform Response Criteria (IMWG), CR: 1) Negative immunofixation on the serum and urine, 2) Disappearance of any soft tissue plasmacytomas and 3) < 5% plasma cells in bone marrow. VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level < 100 mg per 24 hour. The response-evaluable population is defined as participants who received at least 5 of 8 MLN9708 doses in Arm A, at least 2 of 3 MLN9708 doses in Arm B, at least 4 of 5 MLN9708 doses in Arm C, or at least 3 of 4 MLN9708 doses in Arm D and had measurable disease at baseline and at least 1 post-baseline response assessment.

End point type	Primary

End point timeframe:

Day 1 of every other cycle from Day 1 of Cycle 2 (each cycle of 28 days) until death (Up to 5.5 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not reported as only descriptive analysis was performed as planned.

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: percentage of participants				
number (not applicable)	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Inhibition Rate (Emax) (Phase 1)

End point title	Maximum Inhibition Rate (Emax) (Phase 1)

End point description:

Whole blood 20S proteasome inhibition parameters

End point type	Secondary

End point timeframe:

At multiple time points during Cycles 1-3 of each phase and arm of the study, throughout approximately 84-126 days depending on the arm of the study

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: percentage of inhibition				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[3] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[4] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[5] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[6] - Assessment of this endpoint was not performed due to the change in the planned analysis.

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	0[8]	0[9]	0[10]
Units: percentage of inhibition				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[7] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[8] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[9] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[10] - Assessment of this endpoint was not performed due to the change in the planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Occurrence of Emax (TEmax) (Phase 1)

End point title	Time of Occurrence of Emax (TEmax) (Phase 1)

End point description:

Whole blood 20S proteasome inhibition parameters

End point type	Secondary

End point timeframe:

At multiple time points during Cycles 1-3 of each phase and arm of the study, throughout approximately 84-126 days depending on the arm of the study

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: percentage of inhibition				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[11] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[12] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[13] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[14] - Assessment of this endpoint was not performed due to the change in the planned analysis.

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	0[16]	0[17]	0[18]
Units: percentage of inhibition				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[15] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[16] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[17] - Assessment of this endpoint was not performed due to the change in the planned analysis.

[18] - Assessment of this endpoint was not performed due to the change in the planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax: Maximum Observed Plasma Concentration for Ixazomib (Phase 1)

End point title	Cmax: Maximum Observed Plasma Concentration for Ixazomib (Phase 1)

End point description:

The pharmacokinetics (PK) population consisted of all participants who had sufficient dosing data and ixazomib concentration-time data to permit calculation of ixazomib PK parameters. Here, 9999=NA (Standard deviation was not estimable for 1 participant) and 99999=NA (Data was not analyzed for this arm group at this time point).

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and at multiple timepoints (up to 8 hours) on Day 11 for Arm A, Day 15 for Arm B and Day 29 for Arms C and D

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	3	20
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=7,1,2,18,4,6,4,5)|	26.791 (± 18.2608)	39.300 (± 9999)	22.950 (± 9999)	53.278 (± 41.1963)

Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	69.214 (± 30.1985)	22.000 (± 9999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,14,1,0,0,0)|	99999 (± 99999)	99999 (± 99999)	30.267 (± 13.7173)	85.636 (± 64.6346)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	5
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=7,1,2,18,4,6,4,5)|	104.225 (± 46.9148)	55.367 (± 43.8052)	50.875 (± 20.6487)	72.080 (± 54.3984)
Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,14,1,0,0,0)|	285.000 (± 9999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	59.560 (± 37.2229)	109.000 (± 9999)	146.400 (± 90.1703)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Ixazomib (Phase 1)

End point title	Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Ixazomib (Phase 1)

End point description:

The PK population consisted of all participants who had sufficient dosing data and ixazomib concentration-time data to permit calculation of ixazomib PK parameters. Here, 99999=NA (Data was not analyzed for this arm group at this time point).

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and at multiple timepoints (up to 8 hours) on Day 11 for Arm A, Day 15 for Arm B and Day 29 for Arms C and D

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	3	20
Units: hours				
median (full range (min-max))				
Cycle 1, Day 1 (n=7,1,2,18,4,6, 4,5)|	1.020 (0.617 to 4.000)	0.517 (0.517 to 0.517)	1.750 (1.470 to 2.030)	1.000 (0.500 to 2.170)

Cycle 1, Day 1 (n=7,1,2,17,4,6,4, 5)|	319.714 (± 104.6721)	287.000 (± 9999)	450.000 (± 9999)	806.824 (± 472.7173)
Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	1227.143 (± 338.9550)	1180.000 (± 9999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,3,14,1,0,0,0)|	99999 (± 99999)	99999 (± 99999)	705.667 (± 92.5005)	1610.500 (± 770.2156)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	5
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=7,1,2,17,4,6,4, 5)|	1612.250 (± 1009.5816)	662.833 (± 414.5178)	1037.500 (± 397.8748)	934.800 (± 390.2598)
Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,3,14,1,0,0,0)|	1680.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	1527.800 (± 975.9914)	2680.000 (± 9999)	2435.000 (± 1107.5047)

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Rate Constant (λz) for Ixazomib (Phase 1)

End point title	Terminal Elimination Rate Constant (λz) for Ixazomib (Phase 1)

End point description:

Terminal elimination rate constant, calculated as the negative of the slope of the log-linear regression of the natural logarithm concentration-time curve during the terminal phase. The PK population consisted of all participants who had sufficient dosing data and ixazomib concentration-time data to permit calculation of ixazomib PK parameters. Here, 9999=NA (Standard deviation was not estimable for 1 participant) and 99999=NA (Data was not analyzed for this arm group at this time point).

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and at multiple timepoints (up to 8 hours) on Day 11 for Arm A, Day 15 for Arm B and Day 29 for Arms C and D

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	3	20
Units: 1/hour				
arithmetic mean (standard deviation)				

Cycle 1, Day 1 (0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,13,1,0,0,0)|	99999 (± 99999)	99999 (± 99999)	0.004 (± 99999)	0.006 (± 0.0018)
Cycle 1, Day 29 (n=0,0,0,0,0,4,2,4)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	5
Units: 1/hour				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,13,1,0,0,0)|	0.007 (± 9999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 29 (n=0,0,0,0,0,4,2,4)|	99999 (± 99999)	0.005 (± 0.0021)	0.005 (± 9999)	0.006 (± 0.0025)

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Phase Elimination Half-life (T1/2) for Ixazomib (Phase 1)

End point title	Terminal Phase Elimination Half-life (T1/2) for Ixazomib (Phase 1)

End point description:

Terminal phase elimination half-life (T1/2) is the time required for half of the drug to be eliminated from the plasma. The PK population consisted of all participants who had sufficient dosing data and ixazomib concentration-time data to permit calculation of ixazomib PK parameters. Here, 9999=NA (Standard deviation was not estimable for 1 participant) and 99999=NA (Data was not analyzed for this arm group at this time point).

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and at multiple timepoints (up to 8 hours) on Day 11 for Arm A, Day 15 for Arm B and Day 29 for Arms C and D

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	3	20
Units: hours				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11(n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,13,1,0,0,0)|	99999 (± 99999)	99999 (± 99999)	167.000 (± 9999)	130.362 (± 45.0672)
Cycle 1, Day 29 (0,0,0,0,0,4,2,4)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	5
Units: hours				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11(n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,1,13,1,0,0,0)|	98.900 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 29 (0,0,0,0,0,4,2,4)|	99999 (± 99999)	140.575 (± 49.3760)	163.500 (± 9999)	120.050 (± 45.6024)

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Accumulation Ratio for AUCtau (Rac) (Phase 1)

End point title	Observed Accumulation Ratio for AUCtau (Rac) (Phase 1)

End point description:

Accumulation ratio for AUCtau (Rac) was calculated as area under the curve from time zero to end of dosing interval (AUCtau) on Day 14 divided by area under the curve from time zero to end of dosing interval (AUCtau) on Day 1. The PK population consisted of all participants who had sufficient dosing data and ixazomib concentration-time data to permit calculation of ixazomib PK parameters. Here, 9999=NA (Standard deviation was not estimable for 1 participant) and 99999=NA (Data was not analyzed for this arm group at this time point).

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and at multiple timepoints (up to 8 hours) on Day 11 for Arm A, Day 15 for Arm B and Day 29 for Arms C and D

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	3	20
Units: ratio				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	4.019 (± 1.1349)	4.120 (± 9999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,2,12,1,0,0,0)|	99999 (± 99999)	99999 (± 99999)	1.700 (± 9999)	2.288 (± 0.6246)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	5
Units: ratio				
arithmetic mean (standard deviation)				
Cycle 1, Day 1 (n=0,0,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 11 (n=7,1,0,0,0,0,0,0)|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 15 (n=0,0,2,12,1,0,0,0)|	1.970 (± 9999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1, Day 29 (n=0,0,0,0,0,5,2,4)|	99999 (± 99999)	2.632 (± 0.6732)	2.560 (± 9999)	2.540 (± 0.2061)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR is defined as percentage of participants with overall response including CR, VGPR, and partial response (PR). Per IMWG criteria, CR:1)Negative immunofixation on serum and urine, 2)Disappearance of any soft tissue plasmacytomas, 3)< 5% plasma cells in bone marrow. VGPR: Serum+urine M-protein detectable by immunofixation but not on electrophoresis/ 90% or >reduction in serum M-protein + urine M-protein level < 100 mg/ 24-hour. PR:1)≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg/24-hour. If serum+urine M-protein are unmeasurable, ≥50% decrease in difference between involved and uninvolved FLC levels is required. If serum+urine M-protein are unmeasurable and serum free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30%. In addition, if present at baseline, a ≥50% reduction in size of soft tissue plasmacytomas is

required.

End point type	Secondary

End point timeframe:

Day 1 of every other cycle from Day 1 of Cycle 2 (each cycle of 28 days) up to 61 cycles, at end of treatment (Up to 5.5 years)

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	23
Units: percentage of participants				
number (confidence interval 95%)	86 (42 to 100)	67 (9 to 99)	100 (29 to 100)	65 (43 to 84)

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	3	4
Units: percentage of participants				
number (confidence interval 95%)	60 (15 to 95)	40 (5 to 85)	67 (9 to 99)	50 (7 to 93)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Response (Phase 2)

End point title	Time to First Response (Phase 2)

End point description:

Response is defined as CR, VGPR and PR. Per IMWG criteria, CR:1)Negative immunofixation on serum+urine, 2)Disappearance of any soft tissue plasmacytomas, 3)< 5% plasma cells in bone marrow. VGPR: Serum+urine M-protein detectable by immunofixation but not on electrophoresis/ 90% or >reduction in serum M-protein + urine M-protein level < 100 mg/ 24-hour. PR:1)≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg/24-hour. If serum+urine M-protein are unmeasurable, ≥50% decrease in difference between involved and uninvolved FLC levels is required. Else, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30%. In addition, if present at baseline, a ≥50% reduction in size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

From the date of enrollment to the date of the first documented response for up to 5.5 years

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: months				
median (confidence interval 95%)	1.9 (1 to 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) (Phase 2)

End point title	Duration of Response (DOR) (Phase 2)

End point description:

DOR: time of first confirmed PR or better to first PD or start of alternative therapy. DOR was presented for those achieving CR+VGPR+PR, CR+VGPR, and CR. Per IMWG criteria, CR:1)Negative immunofixation on serum+urine, 2)Disappearance of any soft tissue plasmacytomas, 3)<5% plasma cells in marrow. VGPR: Serum+urine M-protein detectable by immunofixation but not on electrophoresis/90% or >reduction in serum M-protein+urine M-protein level <100 mg/24-hour. PR:1)≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90%/to <200 mg/24-hour. If serum+urine M-protein are unmeasurable, ≥50% decrease in difference between involved and uninvolved FLC levels OR ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30%. Also, if present at baseline, a ≥50% reduction in size of soft tissue plasmacytomas is required. Here, 9999=NA(value was not reached due to low number of participants with events).

End point type	Secondary

End point timeframe:

From the time from the date of first documentation of PR or better to the date of first documented disease progression for up to 5.5 years

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: months				
median (confidence interval 95%)	25.2 (4.6 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP) (Phase 2)

End point title	Time to Progression (TTP) (Phase 2)

End point description:

TTP is defined as time from date of enrollment to date of first documented disease progression (PD). Per IMWG criteria, progressive disease requires any 1 or more of following: Increase of ≥25% from nadir in

serum M-component and/or (absolute increase must be ≥0.5 g/dL), urine M-component and/or (absolute increase must be ≥200 mg/24 hour. Participants without measurable serum+urine M-protein levels: difference between involved and uninvolved FLC levels. The absolute increase must be >10 mg/dL. Bone marrow plasma cell percentage: absolute % must be ≥10%. Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in size of existing bone lesions or soft tissue plasmacytomas. Development of hypercalcemia (corrected serum calcium >11.5 mg/dL or 2.85 mmol/L) that can be attributed solely to plasma cell proliferative disorder. Here, 99999=NA (Lower limit of CI was not reached due to the low number of participants with events.).

End point type	Secondary

End point timeframe:

From the date of enrollment to the date of the first documented disease progression for up to 5.5 years

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: months				
median (confidence interval 95%)	22.1 (8.77 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Therapy (Phase 2)

End point title	Time to Next Therapy (Phase 2)

End point description:

Time to Next Therapy is defined as time from the date of enrollment to the date of subsequent antineoplastic therapy.

End point type	Secondary

End point timeframe:

From the date of enrollment to the date of the first documented response for up to 5.5 years

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[19]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[19] - Time to next therapy was not analyzed due to the change in the planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (Phase 2)

End point title	Progression Free Survival (Phase 2)

End point description:

Progression Free Survival is defined as time in months from start of study treatment to first documentation of objective tumor progression per IRF assessment or up to death due to any cause, whichever occurs first. Per IMWG criteria, progressive disease requires any 1 or more of following: Increase of ≥25% from nadir in serum M-component and/or (absolute increase must be ≥0.5 g/dL), urine M-component and/or (absolute increase must be ≥200 mg/24 hour. Participants without measurable serum+urine M-protein levels: difference between involved and uninvolved FLC levels. The absolute increase must be >10 mg/dL. Bone marrow plasma cell percentage: absolute % must be ≥10%. Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in size of existing bone lesions or soft tissue plasmacytomas. Development of hypercalcemia (corrected serum calcium >11.5 mg/dL or 2.85 mmol/L) that can be attributed solely to plasma cell proliferative disorder.

End point type	Secondary

End point timeframe:

From the date of enrollment to the date of the first documented disease progression or death due to any cause for up to 5.5 years

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: months				
median (confidence interval 95%)	18.4 (8.31 to 38.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Phase 2)

End point title	Overall Survival (Phase 2)

End point description:

Overall Survival is the time in months from start of study treatment to date of death due to any cause. Here, 99999=NA (Median and Lower limit of CI was not reached due to the low number of participants with events).

End point type	Secondary

End point timeframe:

From date of enrollment to date of death, approximately 5.5 years (Approximate median follow-up: 43.6 months)

End point values	Arm B: Ixazomib 4.0 mg (RP2D)			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: months				
median (confidence interval 95%)	99999 (34.99 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment.

End point type	Secondary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug or until the start of subsequent antineoplastic therapy for up to 4.9 years

End point values	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg	Arm B: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	3	26
Units: participants				
During Entire Study Any Adverse Event|	7	4	3	26
Grade 3 or Higher Adverse Event|	7	4	3	21
Serious Adverse Event|	2	4	3	12
Adverse Event With Any Study Drug Discontinuation|	0	0	0	8
Adverse Event With Any Study Drug Reduction|	4	2	1	13

End point values	Arm B: Ixazomib 5.5 mg	Arm C: Ixazomib 3.0 mg	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	4	6
Units: participants				
During Entire Study Any Adverse Event|	5	6	4	6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug through 30 days after the last dose of study drug or until the start of subsequent antineoplastic therapy for up to 5.6 years

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Arm A: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle for up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 23 maintenance cycles; overall up to 32 cycles [34 months]).

Reporting group title	Arm A: Ixazomib 3.7 mg

Reporting group description:

Ixazomib 3.7 mg, capsules, orally, on Days 1, 4, 8, 11, 22, 25, 29, 32 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 10 maintenance cycles; overall up to 19 cycles [21 months]).

Reporting group title	Arm B: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 15 maintenance cycles; overall up to 27 cycles [25 months]).

Reporting group title	Arm B: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15 cycle plus melphalan 6 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 49 maintenance cycles; overall up to 61 cycles [58 months]).

Reporting group title	Arm C: Ixazomib 3.0 mg

Reporting group description:

Ixazomib 3.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 30 maintenance cycles; overall up to 39 cycles [40 months]).

Reporting group title	Arm B: Ixazomib 5.5 mg

Reporting group description:

Ixazomib 5.5 mg, capsules, orally, on Days 1, 8, 15 plus melphalan 6 mg/m^2, tablets orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1-4 in 28-day cycle for up to 13 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in

maintenance phase (up to 12 maintenance cycles; overall up to 24 cycles [24 months]).

Reporting group title	Arm C: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 15, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 12 maintenance cycles; overall up to 21 cycles [24 months]).

Reporting group title	Arm D: Ixazomib 4.0 mg

Reporting group description:

Ixazomib 4.0 mg, capsules, orally, on Days 1, 8, 22, and 29 plus melphalan 9 mg/m^2, tablets, orally on Days 1 to 4 and prednisone 60 mg/m^2, tablets, orally, on Days 1 to 4 in 42-day cycle for up to 9 cycles in induction phase followed by ixazomib at dose last tolerated in induction, orally, on Days 1, 8, 15 in 28-day cycle up to 12 cycles or until disease progression or unacceptable toxicity if deriving benefit in maintenance phase (up to 28 maintenance cycles; overall up to 37 cycles [38 months]).

Serious adverse events	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	4 / 4 (100.00%)	3 / 3 (100.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lumbar vertebral fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Seizure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Generalised erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Neurogenic bladder			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm B: Ixazomib 4.0 mg	Arm C: Ixazomib 3.0 mg	Arm B: Ixazomib 5.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 26 (46.15%)	4 / 6 (66.67%)	3 / 5 (60.00%)
number of deaths (all causes)	3	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest injury			

subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

Ileus			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Generalised erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Neurogenic bladder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Femur fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Generalised erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Neurogenic bladder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock	Additional description: One treatment-emergent death occurred in Arm B during treatment with ixazombib 4.0 mg and is not related.		
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A: Ixazomib 3.0 mg	Arm A: Ixazomib 3.7 mg	Arm B: Ixazomib 3.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Plasmacytoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Peripheral venous disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Haematoma			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	3 / 4 (75.00%)	1 / 3 (33.33%)
occurrences (all)	1	3	1
Pyrexia			
subjects affected / exposed	3 / 7 (42.86%)	3 / 4 (75.00%)	1 / 3 (33.33%)
occurrences (all)	14	9	11
Fatigue			
subjects affected / exposed	6 / 7 (85.71%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	17	0	1
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	5
Peripheral swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Feeling cold			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic fatigue syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Feeling hot			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	5	2	1
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Acute pulmonary oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pharyngeal oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Depression			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1

Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	3 / 7 (42.86%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood electrolytes decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza A virus test positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Contusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	2
Clavicle fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Compression fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Synovial rupture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Atrial flutter			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrial tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Peripheral sensory neuropathy			

subjects affected / exposed	4 / 7 (57.14%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	7	5	0
Dizziness			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	4	1	2
Paraesthesia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	5	4	0
Headache			
subjects affected / exposed	1 / 7 (14.29%)	3 / 4 (75.00%)	0 / 3 (0.00%)
occurrences (all)	3	3	0
Neuropathy peripheral			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Neuralgia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Autonomic nervous system			

imbalance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Cognitive disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dementia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness postural			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2

Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	6 / 7 (85.71%)	4 / 4 (100.00%)	2 / 3 (66.67%)
occurrences (all)	18	41	15
Neutropenia			
subjects affected / exposed	5 / 7 (71.43%)	4 / 4 (100.00%)	2 / 3 (66.67%)
occurrences (all)	15	19	6
Anaemia			
subjects affected / exposed	4 / 7 (57.14%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	10	5	1
Lymphopenia			
subjects affected / exposed	3 / 7 (42.86%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	3	19	4
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	8	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ulcerative keratitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 7 (57.14%)	3 / 4 (75.00%)	1 / 3 (33.33%)
occurrences (all)	11	7	1
Nausea			
subjects affected / exposed	6 / 7 (85.71%)	2 / 4 (50.00%)	2 / 3 (66.67%)
occurrences (all)	11	3	4
Vomiting			
subjects affected / exposed	4 / 7 (57.14%)	4 / 4 (100.00%)	1 / 3 (33.33%)
occurrences (all)	6	9	2
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	2 / 3 (66.67%)
occurrences (all)	2	5	2
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Mouth ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3

Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal hernia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastric disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal motility disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematemesis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tongue eruption			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	4 / 7 (57.14%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	23	0	1
Rash maculo-papular			
subjects affected / exposed	3 / 7 (42.86%)	3 / 4 (75.00%)	0 / 3 (0.00%)
occurrences (all)	7	10	0
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Pruritus generalised			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Erythema nodosum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Generalised erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash generalised			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chromaturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pain in extremity			

subjects affected / exposed	3 / 7 (42.86%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	5	1	3
Arthralgia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Arthritis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Myalgia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Polyarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscle swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	2	3
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Klebsiella infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Streptococcal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 7 (57.14%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	12	1	2
Hypokalaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Malnutrition			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4

Non-serious adverse events	Arm B: Ixazomib 4.0 mg	Arm C: Ixazomib 3.0 mg	Arm B: Ixazomib 5.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 26 (100.00%)	6 / 6 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Plasmacytoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 26 (23.08%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	9	0	1
Hypertension			
subjects affected / exposed	4 / 26 (15.38%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	5	0	1
Peripheral venous disease			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 26 (34.62%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	14	1	3

Pyrexia			
subjects affected / exposed	6 / 26 (23.08%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	9	1	2
Fatigue			
subjects affected / exposed	9 / 26 (34.62%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	18	1	0
Oedema peripheral			
subjects affected / exposed	7 / 26 (26.92%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	8	3	3
Peripheral swelling			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	15	0	1
Gait disturbance			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Feeling cold			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chronic fatigue syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Localised oedema			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 26 (34.62%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	10	2	0
Dyspnoea			
subjects affected / exposed	5 / 26 (19.23%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	8	0	1
Catarrh			
subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Epistaxis			
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Respiratory failure			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Dyspnoea exertional			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Acute pulmonary oedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngeal oedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 26 (15.38%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	4	2	2
Depression			
subjects affected / exposed	4 / 26 (15.38%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1
Anxiety			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Confusional state			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Hallucination			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Disorientation			

subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Blood creatinine increased			
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	6	0	0
Platelet count decreased			
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood electrolytes decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Influenza A virus test positive			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

White blood cell count decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Contusion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Clavicle fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Compression fracture			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Face injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Overdose			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)

subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Atrial flutter			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Atrial tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	7 / 26 (26.92%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	12	2	8
Dizziness			
subjects affected / exposed	4 / 26 (15.38%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Paraesthesia			
subjects affected / exposed	5 / 26 (19.23%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Headache			

subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Neuropathy peripheral			
subjects affected / exposed	5 / 26 (19.23%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	7	0	3
Neuralgia			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	2
Dysgeusia			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Somnolence			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Ageusia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Dementia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dizziness postural			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	16 / 26 (61.54%)	5 / 6 (83.33%)	3 / 5 (60.00%)
occurrences (all)	84	18	17
Neutropenia			
subjects affected / exposed	12 / 26 (46.15%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	35	9	17
Anaemia			

subjects affected / exposed	9 / 26 (34.62%)	3 / 6 (50.00%)	5 / 5 (100.00%)
occurrences (all)	26	6	15
Lymphopenia			
subjects affected / exposed	8 / 26 (30.77%)	3 / 6 (50.00%)	2 / 5 (40.00%)
occurrences (all)	33	12	15
Leukopenia			
subjects affected / exposed	7 / 26 (26.92%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	28	9	18
Iron deficiency anaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eyelid oedema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 26 (65.38%)	2 / 6 (33.33%)	5 / 5 (100.00%)
occurrences (all)	38	3	14
Nausea			
subjects affected / exposed	11 / 26 (42.31%)	3 / 6 (50.00%)	3 / 5 (60.00%)
occurrences (all)	19	4	3
Vomiting			
subjects affected / exposed	11 / 26 (42.31%)	1 / 6 (16.67%)	4 / 5 (80.00%)
occurrences (all)	18	4	5
Constipation			
subjects affected / exposed	6 / 26 (23.08%)	3 / 6 (50.00%)	3 / 5 (60.00%)
occurrences (all)	6	4	3
Abdominal pain			
subjects affected / exposed	5 / 26 (19.23%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	12	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	3 / 26 (11.54%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	4	2	0
Abdominal discomfort			
subjects affected / exposed	3 / 26 (11.54%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	6	1	0
Mouth ulceration			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Flatulence			

subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Haemorrhoids			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Odynophagia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Tongue ulceration			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal hernia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastric disorder			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematemesis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tongue eruption			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	10	0	2
Rash maculo-papular			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	4 / 26 (15.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
Rash pruritic			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Alopecia			
subjects affected / exposed	4 / 26 (15.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Erythema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	3 / 26 (11.54%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	5	1	0
Rash papular			
subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0

Dermatitis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Eczema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Generalised erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			

subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Urinary incontinence			
subjects affected / exposed	3 / 26 (11.54%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Dysuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Anuria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chromaturia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 26 (38.46%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	14	0	1
Pain in extremity			
subjects affected / exposed	5 / 26 (19.23%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	6	2	1
Arthralgia			
subjects affected / exposed	6 / 26 (23.08%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	9	5	0
Musculoskeletal chest pain			

subjects affected / exposed	6 / 26 (23.08%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	6	0	0
Arthritis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Bone pain			
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Musculoskeletal pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Flank pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Polyarthritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	8	0	0
Spinal pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Joint swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	0	
Osteoarthritis				
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	0	
Infections and infestations				
Respiratory tract infection				
subjects affected / exposed	3 / 26 (11.54%)	3 / 6 (50.00%)	0 / 5 (0.00%)	
occurrences (all)	4	6	0	
Urinary tract infection				
subjects affected / exposed	6 / 26 (23.08%)	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	6	0	2	
Bronchitis				
subjects affected / exposed	3 / 26 (11.54%)	2 / 6 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	5	4	4	
Upper respiratory tract infection				
subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	4	0	
Pharyngitis				
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	3	0	0	
Herpes zoster				
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	0	2	0	
Oral candidiasis				
subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	1	0	
Oral herpes				
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	0	
Rhinitis				
subjects affected / exposed	2 / 26 (7.69%)	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	0	
Viral infection				
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)	

Rhinrrences (all)

Conjunctivitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Klebsiella infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Diverticulitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Streptococcal infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	4 / 26 (15.38%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	6	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 26 (30.77%)	0 / 6 (0.00%)	3 / 5 (60.00%)
occurrences (all)	9	0	4
Hypokalaemia			

subjects affected / exposed	1 / 26 (3.85%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Hyponatraemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	2 / 26 (7.69%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	3 / 26 (11.54%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Arm C: Ixazomib 4.0 mg	Arm D: Ixazomib 4.0 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Plasmacytoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Peripheral venous disease			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Peripheral coldness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 4 (50.00%)	3 / 6 (50.00%)	
occurrences (all)	4	4	
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 6 (50.00%)	
occurrences (all)	0	3	
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

Oedema peripheral			
subjects affected / exposed	3 / 4 (75.00%)	1 / 6 (16.67%)	
occurrences (all)	4	1	
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Chronic fatigue syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Feeling hot			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Localised oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Catarrh			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Acute pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pharyngeal oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Investigations			
Weight decreased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood electrolytes decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Influenza A virus test positive			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Liver function test increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Clavicle fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Compression fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Face injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Overdose			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Spinal compression fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Synovial rupture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Wrist fracture			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Atrial flutter			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Atrial tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cardiac failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Neuropathy peripheral			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Burning sensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cognitive disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dementia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

Dementia Alzheimer's type			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Dizziness postural			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Memory impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Polyneuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	
occurrences (all)	19	38	
Neutropenia			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	
occurrences (all)	12	35	
Anaemia			
subjects affected / exposed	3 / 4 (75.00%)	4 / 6 (66.67%)	
occurrences (all)	3	7	
Lymphopenia			

subjects affected / exposed	2 / 4 (50.00%)	2 / 6 (33.33%)		
occurrences (all)	9	9		
Leukopenia				
subjects affected / exposed	2 / 4 (50.00%)	4 / 6 (66.67%)		
occurrences (all)	5	15		
Iron deficiency anaemia				
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)		
occurrences (all)	0	0		
Eye disorders				
Blepharitis				
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)		
occurrences (all)	1	0	n	ל

subjects affected / exposed	3 / 4 (75.00%)	3 / 6 (50.00%)	
occurrences (all)	7	10	
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	4 / 6 (66.67%)	
occurrences (all)	2	7	
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	
occurrences (all)	1	6	
Constipation			
subjects affected / exposed	3 / 4 (75.00%)	4 / 6 (66.67%)	
occurrences (all)	4	8	
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Mouth ulceration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Haemorrhoids			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Tongue ulceration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Abdominal hernia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gastric disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Haematemesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Oral pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Tongue eruption			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Erythema nodosum			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Generalised erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Skin hyperpigmentation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Anuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Chromaturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 4 (75.00%)	0 / 6 (0.00%)	
occurrences (all)	5	0	
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	5	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Arthritis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Polyarthritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Muscle swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

Klebsiella infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hordeolum			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Oesophageal candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Streptococcal infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Urethritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	3 / 6 (50.00%)	
occurrences (all)	4	4	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Electrolyte imbalance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Malnutrition			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2011	- Standardized Progression Free Survival and Overall Survival (OS) follow-up to 16 weeks - Revised planned dose level 3 from 5.2 mg to 5.5 mg
29 May 2012	- Clarified that OS visits will be conducted every 16 weeks after document PD, even if participant goes on to receive subsequent treatment - Added Appendices 15.7, Brief Pain Inventory – Short Form; 15.8, World Health Organization Steps of Analgesics and OME Conversions; and 15.10, EORTC Multiple Myeloma Module (QLQ-MY20)
22 March 2013	- Removed the twice-weekly arm (Arm A) from the phase 2 portion of the study - Added 2 new once-weekly 6-week cycle treatment arms to the phase 1 portion of the study (Arm C and Arm D) - Revised the design of the phase 2 portion of the study to include 2 once-weekly treatment arms: one 4-week cycle (Arm B) and one 6-week cycle (Arm C or Arm D) - Updated participant numbers to accommodate new study design (i.e., dropping Arm A and adding Arm C and Arm D) - Extended the induction period of Arm B by 1 cycle (up to 13 cycles) - Removed randomization procedures to be able to enroll participants to phase 2 Arm B in parallel with enrollment to phase 1 Arms C and D

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported